Turkish Journal of Thoracic and Cardiovascular Surgery 2023;31(4):568-572

Case Report / Olgu Sunumu

Systemic capillary leak syndrome during cardiac surgery

Kalp cerrahisi esnasında sistemik kapiller kaçak sendromu

Halil Fatih Aşgün, Sonay Oğuz

Department of Cardiovascular Surgery, Çanakkale Onsekiz Mart University, Faculty of Medicine, Çanakkale, Türkiye

ABSTRACT

Systemic capillary leak syndrome is defined as excessive fluid and protein extravasation caused by microvascular hyperpermeability. It is a very rare condition, and may occur during or after any surgery without preceding symptoms or a suggestive history. It has been reported in pediatric cardiac surgery patients, and is not expected in adults. In this article, we present a 75-year-old female case of severe systemic capillary leak developed during coronary artery bypass grafting combined with dual valve replacement. To the best of our knowledge, this is the first adult case in the literature having an acute attack of systemic capillary leak syndrome during cardiac surgery.

Keywords: Cardiac surgery, cardiopulmonary bypass, capillary leak syndrome, complication.

ÖZ

Sistemik kapiller kaçak sendromu, mikrovasküler hiperpermeabilitenin neden olduğu damar dışına aşırı sıvı ve protein çıkışı olarak tanımlanır. Oldukça nadir olup, bir ön belirti veya düşündürücü bir öykü olmadan herhangi bir cerrahi sırasında veya sonrasında ortaya çıkabilir. Pediatrik kalp cerrahisi hastalarında bildirilmiş olmakla birlikte, erişkinlerde görülmesi beklenmez. Bu yazıda, çift kapak replasmanı ile birlikte koroner arter baypas greftleme esnasında ciddi sistemik kapiller kaçak gelişen 75 yaşında bir kadın hasta sunuldu. Bildiğimiz kadarıyla, bu kalp cerrahisi sırasında sistemik kapiller kaçak sendromunun akut atağı görülen literatürdeki ilk erişkin hastadır.

Anahtar sözcükler: Kalp cerrahisi, kardiyopulmoner baypas, kapiller kaçak sendromu, komplikasyon.

Systemic capillary leak syndrome (SCLS) is a rare condition characterized by massive shift of intravascular fluid and proteins to the interstitium due to microvascular hyperpermeability. Surgery may induce SCLS without a previous history.[1,2] To the best of our knowledge, there is no report regarding SCLS occurred during or after adult cardiac surgery in the literature. In this article, we present an adult case who suffered from an acute SCLS attack during cardiac surgery.

CASE REPORT

A 75-year-old female patient was admitted with non-ST elevation myocardial infarction. The three-vessel coronary artery disease, severe aortic valve stenosis with moderate insufficiency, and moderate mitral valve stenosis were detected. Her preoperative evaluation findings are presented in Tables 1 and 2.

The patient underwent emergent three-vessel on-pump coronary artery bypass grafting (CABG) combined with dual valve replacement due to unstable angina. Cardiopulmonary bypass (CPB) was performed under moderate systemic hypothermia (28ºC) with combined antegrade and retrograde cold blood cardioplegia. Distal anastomosis to the left anterior descending, the obtuse marginal and the right coronary arteries were performed with saphenous vein grafts (SVGs). The aortic and mitral valves had severe fibrocalcification, and the aortic root was too narrow to allow the passage of No. 19 sizer. Root enlargement with Manougian procedure was decided.

Abundant fluid efflux from the SVG harvesting site started at 50 to 60 min of cross-clamp (XCL). Extreme elevation of the diaphragm and insufficient venous return was developed subsequently. Venous cannulas were checked, and found to be at the correct position. The flow of CPB was maintained with replacement of volume expanders, blood and blood products. Aortic valve replacement with root enlargement (No. 21 bileaflet valve in supra-annular position) and mitral valve replacement with total

Corresponding author: Halil Fatih Aşgün.
E-mail: hfasgun@yahoo.com

Doi: 10.5606/tgkdc.dergisi.2023.23712

Received: April 08, 2022
Accepted: May 11, 2023
Published online: October 19, 2023

Cite this article as: Aşgün HF, Oğuz S. Systemic capillary leak syndrome during cardiac surgery. Turk Gogus Kalp Dama 2023;31(4):568-572. doi: 10.5606/tgkdc.dergisi.2023.23712.

Table 1. Results of preoperative evaluation

Examination	Result
Physical examination	Complaints: Dyspnea and chest pain. Comorbidities: Diabetes mellitus, hypertension, moderate chronic obstructive lung disease, anemia, rheumatoid arthritis, hypothyroidism, hypoparathyroidism, vitamin D insufficiency. Preoperative medications: Insulin, metoprolol (25 mg/day), losartan (100 mg), levothyroxine (100 μg/day), ranolazine (375 mg/day), hydroxychloroquine (200 mg/day), tiotropium bromide inhalation (18 μg/day), and combination of formoterol fumarate (24 μg/day) and budesonide (800 μg/day) inhalation. Vital signs: Heart rate 80/min, blood pressure 120/80 mmHg, oxygen saturation on pulsed oximetry 90-95%. Examination: Systolic and diastolic heart murmurs, and basal crackles in both lungs. EuroSCORE II: 25.6%.
ECG	Normal sinus rhythm, heart rate: 75/min, left axis deviation, right bundle branch block.
Chest X-ray	Elevated cardio-thoracic ratio, normal respiratory areas.
Transthoracic echocardiography	Ejection fraction: 55%, left ventricular end-systolic diameter: 33 mm, left ventricular end-diastolic diameter: 44 mm, interventricular septum thickness: 12 mm, posterior wall thickness: 12 mm, left atrial diameter: 44 mm, aortic root diameter: 34 mm, ascending aortic diameter: 39 mm, aortic maximum velocity: 4.2 m/sec, peak transaortic gradient: 70 mmHg, mean transaortic gradient: 45 mmHg, aortic valve area: 0.76 cm^2, peak transmitral gradient: 18 mmHg, mean transmitral gradient: 8 mmHg, moderate aortic valve insufficiency, no mitral regurgitation, no tricuspid regurgitation or stenosis, inferior wall hypokinetic, Stage 1 left ventricular diastolic dysfunction (A>E).
Coronary angiography	Left main coronary artery normal, left anterior descending artery: 99% stenosis, circumflex artery: 70% stenosis, right coronary artery: 95% stenosis, obtuse marginal artery: 90% stenosis.
Carotid artery Doppler ultrasonography	Left common carotid artery: 55-60% stenosis, left internal carotid artery: 60-65% stenosis, right common carotid artery: 55-60% stenosis, normal peak systolic velocity, normal peak end-diastolic velocity, normal resistive index, normal pulsatility index, normal internal carotid artery/common carotid artery ratio, normal vertebral artery direction, diameter and flow.
Spirometry	Forced vital capacity (FVC): 1 L (72.6%), forced expiratory volume in the first second (FEV1): 0.58 L (54.6%), FEV1/FVC: 58.3%.

ECG: Electrocardiogram; EuroSCORE: European System for Cardiac Operative Risk Evaluation.

chordal preservation (No. 25 bileaflet valve) were performed. Elevation of the diaphragm made the exposure and manipulation of the heart quite difficult. Following release of the XCL, cardiac contractions began spontaneously. The total XCL time was 320 min. Ventilation was reinstituted, but the tidal volume was insufficient due to high airway pressure.

The diaphragm was opened through sternotomy. Excess amount of serous fluid similar to pure water was drained. The omentum was extremely edematous and had multiple vesicles. Bilateral pleural spaces were opened, and lots of serous fluid were aspirated. Airway pressure decreased, after pleural and abdominal decompression. A general surgeon was invited. Median laparotomy revealed that omentum, intestines, and retroperitoneal space were extremely edematous. Fluid leakage from the tissue was clearly visible. An abundant amount of fluid was drained. There was no hemorrhage, and SCLS was considered.

Fluid leakage from the wounds, oliguria, and insufficient venous return persisted rest of the surgery. Volume more than 15 L was replaced to maintain CPB flow. To increase intravascular oncotic pressure, 2 U of whole blood, 8 U of erythrocyte suspension, and 4 U of fresh frozen plasma were transfused. Inotropes (20 μg/kg/min dopamine, 20 μg/kg/min dobutamine, 0.2 μg/kg/min adrenaline, and 1.5 μg/kg/min noradrenaline) and intra-aortic balloon pump were provided. Methylprednisolone (125 mg) and theophylline (800 mg) were administered. Following unsuccessful attempts to wean from CPB, the patient was transferred to extracorporeal

Table 2. Results of blood and fluid sample tests

Test	Variables	Preoperative blood	Postoperative blood	Ascites
Blood count	Leucocyte (/μL)	7.01×10^3	12.36×10^3	3
	Hemoglobin (g/dL)	9.1	7,59	-
	Hematocrit (%)	28.3	22,76	-
	Platelet (/μL)	136.2×10^3	18.6×10^3	-
Biochemistry	Glucose (mg/dL)	101.7	180.3	144,1
	Urea (mg/dL)	55.8	24.6	-
	Creatinine (mg/dL)	1.4	1.17	0,68
	Creatinine clearance (mL/min)	35.6	-	-
	Alanine transaminase (U/L)	8.5	87	-
	Aspartate transaminase (U/L)	12.7	199.2	-
	Lactate dehydrogenase (U/L)	319	-	298
	Alkaline phosphatase (U/L)	94	-	-
	Albumin (g/dL)	3.73	0.98	0,83
	Microalbumin (mg/L)	-	-	12,4
	Total protein (g/dL)	6.9	1.72	1,68
	Amylase (U/L)	-	-	15
	Triglyceride (mg/dL)	138.1	-	55,1
	Low-density lipoprotein (mg/dL)	45.5	-	22,2
	High-density lipoprotein (mg/dL)	42.9	-	-
	Sodium (mmol/L)	147	148	146
	Potassium (mmol/L)	4.19	7.04	5,87
	Calcium (mg/dL)	6.32	6.41	-
	Chloride (mmol/L)	100.5	109	110,5
	Magnesium (mg/dL)	1.51	-	-
	Phosphorus (mg/dL)	6.45	-	10
	Creatine kinase-MB (U/L)	166	-	-
	Highly-sensitive troponin I (ng/mL)	0.8	-	-
	Uric acid (mg/dL)	5.3	-	-
	Lactate (mmol/L)	0.8	9.2-17*	-
Hormones	25-OH vit D (ng/mL)	13.8	-	-
	Parathyroid hormone (pg/mL)	29.44	-	-
	Free T3 (pg/mL)	1.82	-	-
	Free T4 (ng/dL)	1.39	-	-
	Thyroid stimulating hormone (μIU/mL)	2.31	-	-
Coagulation	Prothrombin time (s)	17.8 (65%)**	-	-
	International normalized ratio	1.26	-	-
	Activated partial thromboplastin time (s)	34	-	-
Other	C-reactive protein (mg/L)	3.02	-	-
	Erythrocyte sedimentation rate (mm/h)	37	-	-

MB: Myocardial-band; * Minimum and maximum values of multiple measurements, ** Activity.

membrane oxygenation (ECMO) to gain time until capillary leakage recovers. The total CPB time was 690 min. The chest and abdomen were left open.

Generalized body edema, excessive fluid loss from the wounds and the drains (7,250 mL serohemorrhagic fluid within 10 h) persisted during the intensive care unit stay. There was no skin rash. She had profound thrombocytopenia, hypoalbuminemia, and hypoproteinemia. Despite volume replacement (5 U of erythrocyte suspension, 11 U of fresh frozen plasma, and approximately 4,000 mL of autotransfusion blood), ECMO failed due to hypovolemia. The patient died at the postoperative 10th h. Biochemical analysis of the samples revealed exudate fluid (Table 2).

DISCUSSION

Although CPB may cause capillary leak syndrome in pediatric patients, it is unexpected in adults. It has been shown in adults that neither systemic inflammation induced by CPB nor decreased oncotic pressure gradient due to infusions cause protein-rich exudation from the capillary bed.[3] While CPB causes extravasation of water and small solutes, it does not result in transcapillary protein leak and protein-rich exudation. In our case, manifestations were quite dramatic and started at an early stage of surgery. The fluid leakage was so severe that it was visible to the naked eye.

The characteristic triad of SCLS are hypotension, hypoalbuminemia, and hemoconcentration without secondary causes.[4] Similarly, our patient had severe hypotension and severe hypoalbuminemia. However, the last component of the triad, hemoconcentration, was absent. Cardiopulmonary bypass-induced hemodilution, blood loss from the surgical field, and infusions to correct hypovolemia may have prevented the occurrence of hemoconcentration in our case.

Furthermore, our patient had no edema history and the perioperative laboratory results were non-specific. There is no literature evidence of the association between patient's comorbidities and drugs and SCLS. Myxedema was excluded due to normal levels of thyroid hormones. There was no sign of sepsis, anaphylaxis, infection, malignancy, envenomation, and poisoning. Due to the lack of secondary causes, the clinical picture was strongly suggestive for an acute attack of previously unidentified idiopathic SCLS. It is well known that idiopathic SCLS may occur during surgical procedures without preceding symptoms or a suggestive history.[1,2] The rarity and sporadic nature of the condition make it difficult to conclude whether CPB-induced systemic inflammation may have a role in triggering the disease, and whether measures to reduce inflammation including coated circuits, mini-circuits, leukocyte and cytokine filters can prevent the attack.

Management of SCLS is quite troublesome due to the dramatic nature of the disease and the vulnerability of the patients. There is no specific treatment.[4] Fluid management with crystalloids, colloids, and albumin is the mainstay of the treatment. Vasopressors, corticosteroids, and theophylline have been also used in acute attacks.[4,5] High-dose intravenous immunoglobulin (1 to 2 g/kg/day) can be used in prophylaxis and treatment.[4,5] However, there are no data regarding SCLS induced by surgery. Circulatory support with ECMO may give enough time to the patient, until hyperpermeability is resolved.[5]

In conclusion, systemic capillary leak syndrome may develop during cardiac surgery and heavily hamper the procedure. In the current practice, treatment options include fluid replacement, theophylline, high-dose steroids, intravenous immunoglobulin, and circulatory support.

Patient Consent for Publication: A written informed consent was obtained from the patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept: H.F.A., S.O.; Design: H.F.A., S.O.; Data collection: H.F.A., S.O.; Analysis and interpretation: H.F.A., S.O.; Literature review: H.F.A., S.O.; Writing the article: H.F.A., S.O.; Critical review: H.F.A., S.O.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Choi KM, Park CS, Kim MH. Systemic capillary leak syndrome (Clarkson's disease) during elective pylorus-preserving pancreaticoduodenectomy: Case report. Korean J Hepatobiliary Pancreat Surg 2014;18:38-41. doi: 10.14701/kjhbps.2014.18.1.38.
2. Ozawa T, Yamaguchi H, Kiyomatsu T, Saito S, Ishihara S, Sunami E, et al. A case report of idiopathic systemic capillary leak syndrome that occurred during the postoperative period of abdominoperineal resection for colorectal cancer. Int Surg 2015;100:58-62. doi: 10.9738/INTSURG-D-13-00206.1.

3. Tassani P, Schad H, Winkler C, Bernhard A, Ettner U, Braun SL, et al. Capillary leak syndrome after cardiopulmonary bypass in elective, uncomplicated coronary artery bypass grafting operations: Does it exist? J Thorac Cardiovasc Surg 2002;123:735-41. doi: 10.1067/mtc.2002.120348.
4. Druey KM, Parikh SM. Idiopathic systemic capillary leak syndrome (Clarkson disease). J Allergy Clin Immunol 2017;140:663-70. doi: 10.1016/j.jaci.2016.10.042.
5. Juneja D, Kataria S. Capillary leak syndrome: A rare cause of acute respiratory distress syndrome. World J Clin Cases 2022;10:4324-6. doi: 10.12998/wjcc.v10.i13.4324.