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An Unusual Complication of Foam Sclerotherapy: Acute Kidney Injury

Foam Skleroterapiye Bağlı Nadir Bir Komplikasyon: Akut Böbrek Hasarı

ABSTRACT

Sclerotherapy, in which an irritant solution is administered, is a method used to treat venous failure that results in complete venous destruction due to endothelial reaction and fibrosis. In recent years, foam sclerotherapy, in which a sclerosing agent (aethyl sclerole) and air are mixed until they turn into foam and the resultant mixture is injected into noticeable veins directly and into other veins under ultrasonography in doses depending on the diameters of the varices, has been introduced. The drugs or gases used in foam sclerotherapy can cause local or systemic complications. Foam affects vessel endothelial cells and causes severe spasm in the vessel. It has been reported that endothelin-1 levels are high after foam sclerotherapy compared to the initial levels and that neurological complications vary with the endothelin levels. In this report, we present a case of acute kidney injury due to acute tubular necrosis probably caused by endothelin release following foam sclerotherapy.

KEY WORDS: Acute kidney injury, Foam sclerotherapy, Venous insufficiency

ÖZ

Skleroterapi; irritan bir solüsyon aracılığıyla vende oluşan endotelyal reaksiyon ve fibrozisle komplet venöz destrüksiyona neden olarak venöz yetmezliğin tedavisinde kullanılan bir yöntemdir. Son yıllarda gündeme gelen foam skleroterapi yöntemindeyse; sklerozan ajan (aethyl sklerol) ve hava köpük halini alıncaya kadar karıştırılır. Meydana gelen karışım belirgin varislerde direkt, diğerlerinde ise ultrasonografi eşliğinde varislerin çapına göre değişen iğnelerle damara verilir. Foam skleroterapide kullanılan ilaç veya gaza bağlı lokal veya nadiren sistemik komplikasyonlar oluşabilir. Foam, damar endotelyal hücrelere etki ederek damarda yoğun bir spazma neden olmaktadır. Foam skleroterapi sonrası endotelin-1 seviyelerinin başlangıca göre yükseldiği ve gelişen nörolojik komplikasyonların endotelin yüksekliğine bağlı olduğu belirtilmektedir. Biz, foam skleroterapi sonrası endotelin salınımı aracığı ile oluşabileceğini düşündüğümüz "akut tübüler nekroza bağlı akut renal hasar" gelişen bir olguyu sunuyoruz.

ANAHTAR SÖZCÜKLER: Akut böbrek hasarı, Foam skleroterapi, Venöz yetmezlik

INTRODUCTION

Sclerotherapy, in which an irritant solution is administered, is a method used to treat venous failure that results in complete venous destruction due to endothelial reaction and fibrosis. In recent years, a sclerosing solution has been mixed with air in the ratio of one in four and the resultant mixture has been injected (1). Blood is replaced by a sclerosing solution, which directly contacts the vessel wall and influences the endothelial cells, causing severe spasm. In addition to its local effects, it has rare systemic side effects such as pulmonary thromboembolism due to deep vein thrombosis, anaphylaxis and neurological complications. The neurological complications are thought to be due to the cerebral embolus caused by sclerosing substances (2). However, it is also hypothesized that endothelin-1 release leads to neurological complications (3). In this report, we present a case of acute renal injury due to acute tubular necrosis probably caused by endothelin release following foam sclerotherapy.

Müge EREK[1]
Ebru GÖK[2]
Mesudiye BULUT[1]
Didem TURGUT[1]
Nihal ÖZKAYAR[1]
Fatih DEDE[1]

1 Ankara Numune Training and Research Hospital, Department of Nephrology, Ankara, Turkey
2 Dışkapı Yıldırım Beyazıt Training and Research Hospital, Department of Nephrology, Ankara, Turkey

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Correspondence Address:
Müge EREK
Ankara Numune Eğitim Araştırma Hastanesi, Nefroloji Bölümü, Ankara, Turkey
Phone : +90 506 366 50 84
E-mail : drmugeerek@gmail.com

CASE

A 61-year-old male presented to our emergency department with loss of consciousness and weakness. On physical examination, the patient was in moderate general condition with loss of consciousness, blood pressure of 130/80 mmHg, heart rate of 88/min and respiratory rate of 19/min. There were no pathological signs except for pale complexion. The patient did not have a history of chronic diseases and was not taking any medication. He had undergone foam sclerotherapy for varices of his lower extremities at the Cardiovascular Surgery Clinic four days ago. Laboratory investigations showed that hemoglobin was 12 gr./dl, white cell count 6000/mm3, platelet count 320 000/mm3, erythrocyte sedimentation rate 30 mm/hr, CRP 3 mg/L, urea 450 mg/dl, creatinine 24 mg/dl, potassium 8.9 mEq/ L, blood PH 6.9, AST 45 U/L, ALT 23 U/L, CK 81 U/L and myoglobin 60 ng/ml. The patient, whose renal functions had been found to be normal four days ago before administration of sclerosing therapy, was diagnosed with acute renal injury in the Emergency Department and was admitted to the Nephrology Clinic. Urine analysis showed that the urine was light yellow in colour, urine density was 1015, protein was 500 mg/dL, white cell count was 5/High power field (HPF), erythrocyte count was 1/HPF and spot urine protein/creatinine was 1.3 mg/mg. The patient had oliguria with 24-hour urine output of 350 cc and fractional sodium excretion of 2.3%. Renal ultrasonography demonstrated that the size of the kidneys and parenchymal thickness and echogenicity were normal. There were no obstructive lesions or hydronephrosis. Doppler ultrasonography showed that renal vascular structures and filling in the renal arteries and veins were normal and that there were no signs of thrombosis. On MAG3 renal scintigraphy, bilateral renal perfusion was normal but excretion was weak. The patient had hyperkalemia and severe metabolic acidosis. Therefore, we immediately performed hemodialysis through a temporary jugular catheter. Further investigations for possible causes of renal failure showed that serum C3, C4, IgA, IgG and IgM levels were normal and HBsAg, Anti HCV, ANA, Anti DNA, RF, p-c ANCA and Anti-GBM antibodies were negative. No microorganisms were isolated with urine culture. Serum immune fixation electrophoresis and serum light chain levels were normal. Renal biopsy for etiology of acute renal damage revealed that glomerules were normal, but distal proximal tubules were affected and there were signs of acute tubular necrosis including degenerated and necrotic epithelial cells filling the tubular lumens, hyperemic peritubular veins and hemorrhages and basal membrane tears in the tubules. Rhabdomyolysis that is likely to develop after foam sclerotherapy due to intraluminal microthrombosis of the veins was excluded by the normal urine analysis and muscle enzymes and the lack of myoglobin plugs on renal biopsy. The history did not reveal any herbal product or substance use except for the administration of sclerotherapy for a few days. Patient records kept at the Cardiovascular Surgery Clinic revealed that perioperative and intraoperative blood pressures were normal, transfusion had not been required after sclerotherapy and no antibiotics or nonsteroidal anti-inflammatory drugs had been used. There was edema in the left lower extremity. We performed arterial Doppler examination of bilateral extremities and found no abnormalities. Doppler ultrasonography of the venous system demonstrated an increase in the left popliteal vein calibration and echogenicity in the lumen, suggestive of subacute deep vein thrombosis. Pulmonary scintigraphy and blood trophonine levels did not suggest pulmonary embolus. In addition to elevation of the lower extremities, subcutaneous low molecule heparin was initiated. Repeated renal Doppler ultrasonography and scintigraphy showed that renal perfusion and filling of the renal arteries and veins were normal. Renal function tests were performed and oral intake and excretion were followed daily to determine whether renal replacement therapy was necessary. The patient underwent a total of three sessions of hemodialysis, which caused a rapid improvement in renal functions. In fact, renal functions returned to normal within one week of admission (serum creatinine: 1 mg/dl) and the patient did not need hemodialysis any longer. Evaluation of the findings excluded prerenal causes, rhabdomyolysis, systemic diseases, vascular pathologies, glomerular disease and nephrotoxic substance use except for sclerotherapy. The patient was diagnosed with acute tubular necrosis and acute renal injury due to sclerotherapy. He was discharged and kept under regular supervision.

DISCUSSION

Chronic venous failure is an important health problem since its diagnosis and treatment are costly (4). The best-known risk factors are genetic tendency, long-term standing, trauma to lower extremities, obesity, and pregnancy (5). Initial treatment of chronic venous diseases is with preventive measures such as reaching an ideal weight and avoiding tight clothing (6). Endoablation, in which superficial veins are exposed to sclerotherapy with laser or chemical agents, is the surgical treatment of choice at present. In recent years, foam sclerotherapy, in which a sclerosing agent (aethoxy-sclerol) and air are mixed until they turn into foam and the resultant mixture is injected into noticeable veins directly and into other veins under ultrasonography in doses depending on the diameters of the varices, has been introduced (7).

Local or systemic complications may develop due to the drugs or gases used in foam sclerotherapy. In addition to cosmetic complications such as telangiectasia (15%-24%) and pigmentation (10%-30%), systemic complications may also develop. It has been reported that deep vein thrombosis (1%-3%), stroke (0.01%), superficial vein thrombosis (4.4%), tissue necrosis (in varying rates), edema (0.5%) and nerve damage (0.2%) may occur (8).

The sclerosing substance used in the procedure replaces blood in the vessel lumen and thus directly contacts the vessel wall. In foam sclerotherapy, intraluminal minimal thrombosis

related panmural damage is created as a result of damage to the intima of the vein wall and collagen denaturation in the media. The thrombosis turns into fibrous occlusion in the vein lumen in cases in which sclerotherapy is successful (9). Differential diagnosis of the etiology of acute kidney injury in our case included rhabdomyolysis developing after intraluminal minimal thrombosis in the vein due to foam. However, lack of abnormal signs of muscle damage (CK, myoglobin) and myoglobin plugs in renal biopsy and light yellow urine colour excluded rhabdomyolysis. Foam affects vessel endothelial cells and causes severe spasm in the vessel. It has been reported that endothelin-1 (ET-1) levels are high after foam sclerotherapy compared to the initial levels and that neurological complications vary with endothelin levels (3). Endothelin-1 is a vasoconstrictor peptide synthesized from hepatic endothelial, epithelial and smooth muscle cells. Its secretion is stimulated by hypoxia, dehydration, endotoxin and baroreceptor activation (10). ET-1, a powerful proinflammatory and pro-fibrotic vasoconstrictor peptide, is thought to play an important role in most of the pathologies in acute kidney injury (11). Kidneys are more susceptible to the vasoconstrictor effect of ET-1 than other vascular areas (12,13). As an effective vasoconstrictor, ET-1 has been shown to decrease blood flow and glomerular filtration rates. In one study, a change in affinity of ET-1 marked with I125 in renal receptors following ischemia was shown while increased ET-1 was shown to cause acute kidney injury in another study on rats (14,15).

Avoiding high volumes in foam sclerotherapy can help to prevent possible thrombosis and other complications (16). In the case presented here, the development of acute renal injury can be attributed to the volume used and the fact that kidneys are more sensitive to vasoconstrictor effects of ET-1 than other vascular beds in the absence of systemic effects including hypertension and neurological complications likely to be due to ET-1 secretion.

Renal vasoconstriction due to increased ET-1 might have played a role in acute tubular necrosis developing after sclerotherapy. In the case presented here, acute kidney injury developed after foam sclerotherapy, which is still a popular method used to treat varices. Taking into account the possibility of development of systemic complications likely to affect morbidity and mortality in addition to local complications, the perioperative follow-up of patients is of great importance.

REFERENCES

1. Heck M, Faulhaber J, Breu FX, Schneider SW: Foam sclerotherapy: Uses and indications in dermatology and phlebology. Hautarzt 2012; 63(6):493-505
2. Hanisch F, Müler T, Krivokuca M, Winterholler M: Stroke following variceal sclerotherapy. Eur J Med Res 2004; 9:282
3. Frullini A, Barsotti MC, Santoni T, Duranti E, Burchielli S, Di Stefano R: Significant endothelin release in patients treated with foam sclerotherapy. Dermatol Surg 2012; 38(5):741-747
4. Nicolaides AN, Allegra C, Bergan J, Bradbury A, Cairols M, Carpentier P, Comerota A, Delis C, Eklof B, Fassiadis N, Georgiou N, Geroulakos G, Hoffmann U, Jantet G, Jawien A, Kakkos S, Kalodiki E, Labropoulos N, Neglen P, Pappas P, Partsch H, Perrin M, Rabe E, Ramelet AA, Vayssaira M, Ioannidou E, Taft A: Management of chronic venous disorders of the lover limbs: Guidelines according to scientific evidence. International Angiology 2008; 27:1-59
5. Jawien A: The influence of environmental factors in chronic venous insufficiency. Angiology 2003;54 Suppl 1: S19-31
6. Eberhardt RT, Raffetto JD: Chronic venous insufficiency. Circulation 2005; 111;2398-2409
7. Bhogal RH, Moffat CE, Coney P, Nyamekye IK: Can foam sclerotherapy be used to safely treat bilateral varicose veins? Phlebology 2012; 27 (1):19-24
8. Asciutto G, Lindblad B: Catheter-directed foam sclerotherapy treatment of saphenous vein incompetence. Vasa 2012;41(2):120-124
9. Tessari L, Cavezzi A, Frullini A: Preliminary experience with a new sclerosing foam in the treatment of varicose veins. Dermatol Surg 2001; 27:58-60
10. Trevisani F, Colantoni A, Gerbes AL, Gülberg V, Sica G, Caraceni P, De Notariis S, Morselli-Labate AM, Ligabue A, Gasbarrini G, Bernardi M: Daily profile of plasma endothelin-1 and -3 in pre-ascitic cirrhosis relationship with arterial pressure and renal function. J Hepatol 1997; 26; 808-815
11. Neuhofer W, Pittrow D: Role of endothelin and endothelin receptor antagonists in renal disease. Eur J Clin Invest 2006; 36 Suppl 3:78-88
12. Loutzenhiser R, Epstein M, Hayashi K, Horton C: Direct visualization of effects of endothelin on the renal microvasculature. Am J Physiol 1990; 258: F61-68
13. Rabelink TJ, Kaasjager KA, Boer P, Stroes EG, Braam B, Koomans HA: Effects of endothelin-1 on renal function in humans: Implications for physiology and pathophysiology. Kidney Int 1994;46:376-381
14. Itoh S, Sasaki T, Ide K, Ishikawa K, Nishikibe M, Yano M: A novel endothelin ETA receptor antagonist, BQ 485, and its preventive effects on experimental cerebral vasospasm in dogs. Biochem Biophys Res Common 1993; 195:969-975
15. Ruschitzka F, Shaw S, Gygi D, Noll G, Barton M, Lüscher TF: Endothelial dysfunction in acute renal failure: Role of circulating and tissue endothelin-1. J Am Soc Nephrol 1999; 10(5):953-962
16. Cavezzi A, Parsi K: Complications of foam sclerotherapy. Phlebology 2012; 27 Suppl 1:46-51