

Reversible diffuse arterial spasm in a patient with primary oxalosis

Primer oksalozisli bir hastada tersinir yaygın arteriyel spazm

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In this article, we report a 22-year-old female case with primary oxalosis type 1 who was admitted with ischemic lower extremities. The arteriogram revealed diffuse arterial narrowing involving the abdominal aorta, iliac arteries and lower limb arteries. Continuous nitroprusside infusion resulted in immediate relief of ischemic symptoms. She was put on nifedipine treatment which resulted in improved walking ability and increased vascular calibration on her follow-up. The instant onset of action and rapid improvement of symptoms recommend nitroprusside trial in oxalosis patients with vascular symptoms.

Key words: Arterial vasoconstriction; blood vessels; nifedipine; nitroprusside; oxalosis.

Primary hyperoxaluria is a rare autosomal recessive disorder characterized by calcium oxalate (CaOx) nephrocalcinosis and progressive renal failure. Although urolithiasis and renal failure are generally the first manifestations of the disease, other organs such as the heart, vessels, skin, and bone may also be affected by the widespread deposition of the oxalate crystals throughout the body. There is no satisfactory modality for the long-term therapy of the disease, and more than 80% of the patients die from renal failure before the age of 20.^[1] We report here on a patient with oxalosis who presented with diffuse arterial spasm that partially reversed with the use of vasodilating drugs.

CASE REPORT

A 22-year-old female was admitted to our hospital with ischemic changes in both lower extremities. Her feet were painful, cold, and pulseless. The femoral

Bu yazıda, alt ekstremitte iskemisi ile başvuran primer oksalozis tip 1'li 22 yaşında kadın olgu sunuldu. Hastanın arteriyogramlarında abdominal aort, iliyak arterler ve alt ekstremitte arterlerinde yaygın arteriyel daralma görüldü. Sürekli nitroprusid infüzyonu iskemik semptomlarında ani rahatlama sağladı. Takipte yürütme kapasitesinde iyileşme ve damar kalibrasyonunda artış ile sonuçlanan nifedipin tedavisine başlandı. Ani hastalık başlangıcı ve semptomlarda hızlı iyileşme sağlayan nitroprusid infüzyonu, vasküler semptomları olan oksalozis hastalarında denenebilir.

Anahtar sözcükler: Arteriyel vazokonstriksiyon; kan damarları; nifedipin; nitroprusid; oksalozis.

artery pulses were barely palpable, and there were no popliteal and distal posterior tibial artery pulses. Angiography revealed diffuse and smooth narrowing of the abdominal and pelvic arteries, and the superficial femoral arteries were also diffusely narrowed (Figure 1). However, there were no occlusions or collaterals. The abdominal aorta and common iliac arteries were 10 mm and 4 mm in diameter, respectively. The attenuation of the vessel caliber became gradually more prominent to the distal branches and hindered visualization of the infrapopliteal arteries, although there was no occlusion. The infrapopliteal arteries could faintly be visualized only after papaverine infusion (Figure 2).

The patient had a history of extracorporeal shockwave lithotripsy at the age of seven and 21; however, she underwent no further evaluation and was diagnosed with idiopathic nephrolithiasis. Apart from that, she was apparently in good health until she



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Figure 1. Angiography shows the diffuse and smooth narrowing of the (a) abdominal aorta, (b) pelvic arteries and (c) femoral arteries. Note that the superficial femoral arteries are barely visible (arrows).

got pregnant four years prior to her admission to our facility. Her renal functions had progressively declined since then, and she had been on hemodialysis for the previous two years.

During her hospitalization, she was found to have splenomegaly and bilateral nephrolithiasis. Her left atrium and ventricle were dilated, and there was mitral, aortic, and tricuspid valve regurgitation. She also had diffuse sensorineural polyneuropathy. Laboratory investigations revealed negative cytoplasmic-antineutrophil cytoplasmic antibodies (cANCA), perinuclear-antineutrophil cytoplasmic antibodies (pANCA), antimitochondrial antibodies, antinuclear antibodies, anti-smooth muscle antibodies, and cryoglobulin. Her complete blood count was within normal limits. The C-reactive protein (CRP) levels (50 mg/l) and erythrocyte sedimentation rate (ESR) (59 mm/hour) were elevated. In addition, the serum creatinine (5.7 mg/100 ml), blood urea nitrogen (46 mg/100 ml) and serum potassium (5.6 mEq/l) levels were also elevated, but the serum calcium levels were normal (9 mg/100 ml). A bone marrow biopsy revealed oxalate crystals. Although the patient tested negative for the G170R mutation in the alanine: glyoxylate aminotransferase (AGT) gene, she was diagnosed as having type 1 primary hyperoxaluria owing to the severity of the disease and the fact that the gene mutation is positive in only 50% of the cases.^[2]

The patient was given continuous intravenous nitroprusside infusion, and the starting dose of 0.5 $\mu\text{m}/\text{kg}/\text{minute}$ resulted in immediate relief of the pain and coldness. With a dose of 2 $\mu\text{m}/\text{kg}/\text{minute}$, she was asymptomatic, and the dorsalis pedis pulses returned. On follow-up, she was put on treatment with nifedipine, losartan, pregabalin, and epoetin. This was followed by a satisfactory

circulatory status of the extremities. On her physical examination performed two months later, there were normal to weak femoral and popliteal pulses along with diminished distal posterior tibial and dorsalis pedis artery pulses. Although the patient stated that she had significant improvement in her ability to walk, she still complained of intermittent claudication. Therefore, she was included on the transplantation recipient list for renal, liver, and cardiac transplantation. Computed tomography (CT)



Figure 2. Two views of the right infrapopliteal arteries are shown after the contrast injection from the 4F introducer was placed in the right common femoral artery. (a) There is no visible filling of the infrapopliteal arteries before papaverine injection. (b) The infrapopliteal arteries can faintly be seen after the papaverine injection.



Figure 3. Computed tomography angiography two months later reveals the increase in diameter of the abdominal aorta and iliac artery.

angiography obtained for preoperative evaluation for transplantation revealed increased abdominal aorta (15 mm) and external iliac artery (9.5 mm) diameters (Figure 3). Furthermore, her Doppler ultrasound examination revealed patent lower extremity arteries with monophasic flow patterns in the infrapopliteal arteries.

DISCUSSION

Vascular complications are common in advanced primary hyperoxaluria, with Raynaud's phenomenon, livedo reticularis, distal ischemia, and peripheral gangrene being reported most often.^[3-7] Although the exact mechanism is unknown, *in vitro* studies suggest CaOx crystals initiate vascular damage by triggering polymorphonuclear leukocyte-mediated endothelial cell injury, leading to vascular spasm and thrombosis.^[8] The histopathological findings include crystal deposition in the muscular layer, subintimal fibrosis, and crystals that occlude the arterioles.^[3,4,8]

Although reversible diffuse vascular spasm in young adults is frequently a complication of ergot alkaloid usage for migraines and is reversible with the cessation of the drug, there have also been some reports of severe diffuse vascular narrowing in patients with chronic renal insufficiency and nephrolithiasis due to oxalosis. In all of these cases, the symptoms were present on all of the extremities, and the vascular narrowing was irreversible and occurred as a result of extensive calcification of the arteries.^[3-6,9] In our case, the symptoms were limited to the lower limbs. There was no visible calcification of the arteries, and

the symptoms improved with the use of vasodilating drugs. In this manner, it was similar to arterial spasm in ergotism which favors symmetrical involvement of the lower extremities that can be reversed with nifedipine.^[9] However, our patient had no history of ergotamine usage but had bilateral nephrolithiasis and chronic renal insufficiency like the oxalosis patients. There is only one reported case of oxalosis with diffuse narrowing of the arteries that partially recovered with the use of nitroprusside and completely reversed after renal transplantation. No vascular calcifications were noticed in that patient either.^[10] The previous reports on vascular insufficiency in oxalosis patients make it logical to assume that the cause of vascular spasm in our case might have been oxalosis. Oxalate deposition in the vascular smooth muscle could have been the reason for the vascular spasm. Presumably, accumulation of more oxalate crystals in a later stage could have led to irreversible ischemia with gangrene.

Peripheral vascular insufficiency can be devastating in oxalosis patients. Dialysis, heparin, steroids, phenoxybenzamine, vasodilators, epidural blocks, lumbar sympathectomies, and hyperbaric oxygen have been unsuccessful in treatment.^[3,4] There have been only two cases that were treated with nitrates.^[7,10] Our patient also had significant recovery from ischemia after the nitroprusside infusion. The instant onset of action and rapid improvement of symptoms recommended by this nitroprusside trial may be beneficial for oxalosis patients with vascular symptoms in the future.

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