Amlodipine Induced Massive Ascites, a Rare Clinical Case

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Introduction. Calcium channel blockers (CCBs) are commonly used agents in the treatment of hypertension as part of monotherapy or combination therapy. Peripheral edema is the most common side effect that requires discontinuation or replacement of treatment. Some studies in the literature have shown that long-acting dihydropyridine type CCBs lead chylous ascites in peritoneal dialysis patients. However, amlodipine-associated serous ascites cases are not available in the literature.

Case Report. In this case report, we describe a rare case of amlodipine induced massive ascites in a 30-year-old male with renal transplantation.

Conclusion. We aimed to create awareness that pharmacologic causes should be considered in cases of ascites of unknown aetiology.

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Case Report

INTRODUCTION

Calcium channel blockers (CCBs) are drugs that prevent calcium flow through ion-specific channels in the cell membrane commonly used in the treatment of hypertension,[1] angina pectoris[2] and cardiac arrhythmias.[3] Amlodipine is a dihydropyridine type CCBs which inhibits the L-type calcium channels on the cells and relaxes the vascular smooth muscle cells, leading to decreased blood pressure by generating vasodilation and diminishing peripheral vascular resistance selectively on afferent side of the capillary network. Increased blood flow of afferent side may lead to peripheral edema, the most common side effect of CCBs.[4] However, amlodipine-associated serous ascites information is not available in the literature.

CASE REPORT

A 30-year-old male patient who was diagnosed with end-stage renal failure 10 years ago due to hypertensive nephrosclerosis was admitted to our clinic with complaints of abdominal distention and pain accompanied by weight gain. The patient had a kidney transplant from a living donor 5 years ago. On physical examination, blood pressure was 130 / 80 mmHg, abdomen was distended and there was a scar in the right lower quadrant due to renal transplant operation. There was no significant difference in other findings. The patient was using tacrolimus 2.5 mg/d, mycophenolic acid 720 mg/d, prednisolone 2.5 mg/d, acetyl salicylic acid 100 mg/d, carvedilol 12.5 mg/d, clopidogrel 75 mg/d, and amlodipine 10 mg/d. As the abdominal ultrasound imaging revealed, there was free fluid in the abdomen, liver size was normal, surface was smooth, parenchyma was homogeneous. The patient was hospitalized for investigation of the etiology of ascites. In the chemical analysis of the ascites made for diagnostic purposes, total protein was determined as 0.8 g/L, albumin was 0.7 g/L, and LDL was 26 U/L. At the same time, serum albumin was 4.4 g/dL, total protein was 6.9 g/dL, serum urea was 46 mg/dL, and creatinine was 2.63 mg/dL. Liver function tests were within normal ranges. PT was 11 seconds (INR = 0.96). In urine test nitrite and protein was negative, erythrocyte and leukocyte was 0, PH was 6.5 and density was 1017. Transthoracic echocardiography results were normal: ejection fraction was 65%, pulmonary artery pressure was 25 mmHg, heart valve movements, and mitral-aortic valve thicknesses were normal, and no pericardial

fluid was detected. Pulmonary X-ray imaging was normal. Portal doppler ultrasonography revealed that hepatic vein flow was hepatofugal and vena cava inferior flow was normal. There was no varicose vein on upper gastrointestinal endoscopy. With these findings the patient was consulted to the gastroenterologist. The gastroenterologist stated that the ascites was not associated with liver pathologies due to the absence of pathology in liver ultrasound findings, normal albumin and INR levels, normal liver function tests, no varicose veins in the upper gastrointestinal endoscopy, and normal portal doppler ultrasound. Patient's amlodipine was discontinued. Because CCB-related peripheral edema mechanism is capillary hydrostatic pressure increase due to arterial dilation and because we could not find another etiological cause in the patient, we decided to discontinue amlodipine. In order to regulate blood pressure in the patient, we increased the dose of beta blocker instead of amlodipine. His symptoms regressed in the first week after discontinuation of amlodipine and it was observed that the fluid decreased in the ultrasound. Ultrasonography performed at the end of second month revealed that the ascites in the patient completely regressed.

DISCUSSION

Dihydropyridine calcium channel blockers (CCBs) are drugs that are often used in the treatment of hypertension. The most common side effect of these agents is peripheral edema with an estimated incidence of 12%.[5] Dose reductions or discontinuation and an alternative antihypertensive medication should be recommended in these patients.[5,6] Dilating afferent side of capillary network and causing increasing capillary hydrostatic pressure are the main mechanisms of edema.[7] Non-cardiogenic pulmonary edema is also unexpected and a rare complication in amlodipine poisoning.[8,9] It has the same mechanism with precapillary vasodilation. In the literature there are rare case reports of chylous ascites associated with lercanidipine, characterized by greater lipophilicity than other dihydropyridines, especially in patients that are receiving peritoneal dialysis.[10,11] The exact mechanism is unknown but Yang *et al.* hypothesized that lercanidipine may affect smooth muscle cells of blood and lymphatic vessels.[12] In addition to that, peritoneal lymphovascular dilatation due to CCBs is described as a possible mechanism.[13]

There is only one case report with manidipine induced spontaneous chyloperitoneum in systemic lupus erythematosus patient that isn't receiving PD.[14] However, no case of transudate ascites with amlodipine have been observed in the literature.

Ascites is caused by the abnormal accumulation of fluid within the peritoneal cavity. The most common reasons of ascites are cirrhosis-induced portal hypertension, malignancy and heart failure.[15] In addition to that, ascites can be due to many different etiological reasons such as hypoalbuminemia, peritoneal disease and other rare etiologies (myxedema, abdominal pregnancy, whipple disease and sarcoidosis etc.).[16]

CONCLUSION

To the best of our knowledge, our case is the only case reported in the literature that indicates ascites associated with amlodipine usage. We excluded the most frequent causes, thus amlodipine was identified as the etiology of this rare condition. The patient, who was on follow-up for 10 months, didn't repeat the ascites after discontinuation of the drug. We need further studies to identify the exact mechanism of this adverse effect.

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