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A Case of Furosemide Induced Nephrocalcinosis

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Abstract

Background: Although furosemide is widely used for various medical conditions in adults, its association with nephrocalcinosis is not well established. In adults, nephrocalcinosis induced by furosemide is rare condition and presents as medullary nephrocalcinosis without significant alteration of renal function.

Methods and Results: A 50-year-old female patient was admmited at our department due to renal insufficiency (creatinine clearance was 62 mL/min) of unknown etiology. In medical history of the patient, drug abuse was verified with a daily intake of 160 mg of furosemide during four years. The reason of selfinitiated excessive furosemide intake was allegedly face and limb swelling. Patient denied any previous kidney disease. The patient was normotensive with completely normal physical status. Both, blood count and urinalysis were normal. Blood pH value was 7.43 and urine pH value was 6.5. Amount of 24h urine proteinuria was 200 mg. Electrolites and urine acid concentrations in blood and in 24h urine sample were normal. Serum levels of renin and aldosteron as well as their ratio were regular. Urine concentration test showed izostenuric values. At sonography, normal shaped and sized kidneys were found, with reduced parenchyma and a diffuse increase in echogenicity throughout the medullary pyramids. By CT imaging, diffusely distributed soft tiny calcifications of kidneys medulla were identified. In kidney biopsy samples, medulla calcifications (both in tubuli and interstitium) were described.

Conclusion: In conclusion, we can address that in our patient broad diagnostic procedure was performed in a way we could exclude various causes of nephrocalcinosis. In adults with nephrocalcinosis, besides many disorders, furosemide abuse should be considered as a potential etiopatogenetic factor.

Keywords: Adults; Furosemide; Nephrocalcinosis; Renal insufficiency; Ultrasonography

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Introduction

Nephrocalcinosis, the abnormal deposition of calcium salts in the renal parenchyma, is a rare disease [1]. It can take two different forms: medullary nephrocalcinosis is the most frequent form and is characterized by the exclusive involvement of the medullary pyramids. In a diffuse or cortical nephrocalcinosis, which is rare, the entire parenchyma is affected: this pattern is associated with severe metabolic disorders, such as hyperoxaluria, or end-stage nephropathy [2].

The association between nephrocalcinosis and long-term furosemide therapy is well documented in infants [3]. Pyramidal involvement is present in more than 60% of preamature infants with low birth weight or full term infants with congestive heart failure, treated with furosemide for long periods. Although furosemide is widely used for various medical conditions in adults, its association with nephrocalcinosis is not well established. In adults, nephrocalcinosis induced by furosemide is rare and presents as medullary nephrocalcinosis without significant alteration of renal function. So far, only a few cases of nephrocalcinosis caused by furosemide in adult patients have been described in the literature, but just one of them included either imaging description of kidney and histological documentation of the kidney biopsy [2].

A 50-year-old female patient was admitted to our hospital for investigation of azothaemia. She was seen in another hospital for facial edema and swelling of the fingers and knees, and later was referred to our hospital for further evaluation. In previous medical history, she had tonsillectomy, fracture of left hand in a traffic accident. The patient entered menopause in her 37th year and was taking oral hormonal supplementation only for several months. Three years before admission she

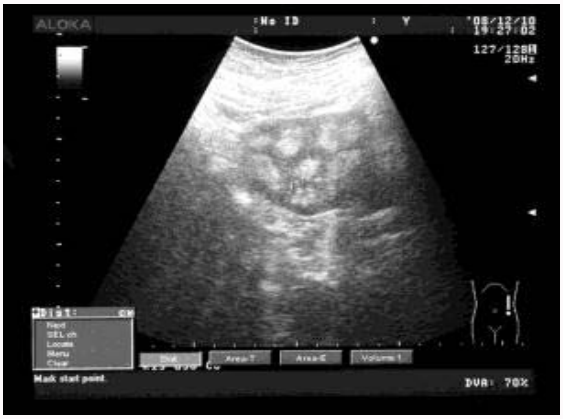

Figure 1: US kidney examination: diffuse pyramidal calcium deposits.

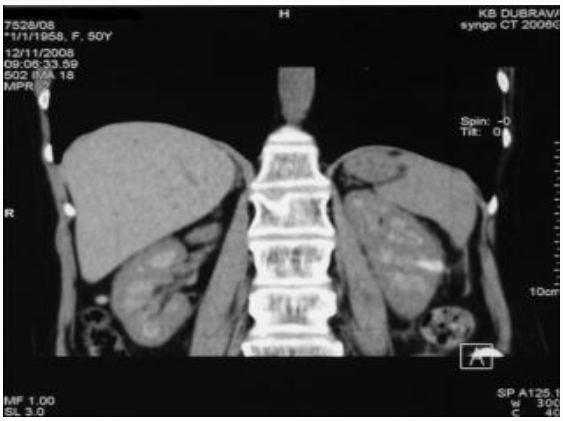

Figure 2: CT kidney examination: tiny medullary hyperechogenicity.

had a parodontosis of upper teeth. During past several years she has been occasionally suffering from insidious lumbar pain. The patient has been self-administering furosemide 160mg/day for 4 years due to persistent facial and knee edema and allegedly low daily urine volume. Two weeks before hospitalization at our department she had cancelled furosemide intake according to advice of her general practitioner.

Methods and Results

On admission the patient was 161cm tall, weighted 53 kg and had high blood pressure (170 mmHg/110 mmHg). No edema was observed and physical examination was normal. We performed a broad laboratory analysis. Both, blood count and urinalysis were normal. Blood pH value was 7.43 and urine pH value was 6.5. Urine microbiology was sterile. Amount of 24h urine proteinuria (determined by Biuret test) was 200 mg. Initial metabolic evaluation was performed: concentration of creatinine, calcium, phosphorus, uric acid, sodium, potassium and chloride were measured both in blood and urine. 24-urine samples were also analyzed for volume, magnesium, oxalate and citrate.

Renal function was depressed (creatinine clearance was 62 ml/min). All the other parameters analyzed were normal. A parathyroid ultrasound was normal. Intact PTH was measured in the blood which was normal. Serum levels of renin and aldosteron as well as their ratio were regular. Urine concentration test showed izostenuric values (in first urine sample osmolality was 290 mOsm/L). Finally, we decided to make radio morfological and pathohistological investigation.

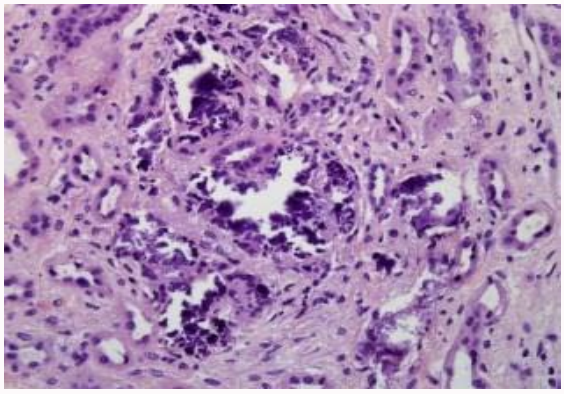

Figure 3: Only few cortical tubules.

We used Simens acuson ultrasound device and Siemns Somatom Sensation 16 CT system. A renal ultrasound showed medullary nephrocalcinosis with total involvement of medullary pyramids (Figure 1). An abnormal renal computerized tomography confirmed this sonographic finding (Figure 2).

Biopsy findings

Three peaces of kidney tissue measuring 4-10 mm were analyzed. About 70% of tissue was medulla and the rest was cortex with 11 glomeruli. Two glomeruli were globally sclerotic and the all others had normal morphology. There were several foci of calcification in tubules and interstitium predominantly within medulla (Figure 3). Only few cortical tubules were involved by calcification. The all others cortical tubules had normal morphology. The foci of calcification were surrounded by interstitial fibrosis and tubular atrophy. The blood vessels were unremarkable. There was no evidence of immune deposits in immunofluorescent stains and electron microscopy demonstrated the normal ultra structure of analyzed glomerulus and surrounding tubules.

Clinical follow-up

Two months after discharged from hospital, patient came to first control examination. In laboratory findings there were 24h proteinuria level of 0.7 g and better renal excretion parameters: serum creatinine 83 μmol/L with creatinine clearance of 72 mL/min and normal serum potassium level (4.5 mmol/L).

Discussion

Nephrocalcinosis, is a term originally used to describe deposition of calcium salts in the renal parenchyma due to hyperparathyroidism. It is now more commonly used to describe diffuse, fine, renal parenchymal calcification on radiology. Nephrocalcinosis can be subdivided into the cortical type, which is classically the result of acute tubular necrosis, and the medullary type seen in several metabolic disorders. Many causes of nephrocalcinosis have been added since the original description. These include causes of hypercalcemia and hypercalciuria, medullary sponge kidney, hyperparathyreoidism, renal tubular acidosis (RTA) specifically distal RTA, renal tuberculosis, renal papillary necrosis, oxaluria, sarcoidosis and milk-alkali syndrome [4-7]. Furosemide is a powerful diuretic drug which has been used successfully in the treatment of congestive heart failure. Hyponatremia, hypokalemia and metabolic alkalosis are frequent side-effects of the treatment. An association of renal calcinosis with furosemide therapy in preterm infants was first reported in the early 1980's, the risk of developing nephrocalcinosis being highest

in the most premature ones. Furthermore, the risk of developing nephrocalcinosis was correlated with the dose of furosemide [2]. In addition to, the period soon after initiation of furosemide therapy appears most sensitive in regard of developing nephrocalcinosis [2]. The calciuric action of furosemide is one of the most distinguished factors provoking nephrocalcinosis in preterm infants, but other provoking pathogenic mechanisms are undoubtedly also involved in most cases. Human and animal studies suggest that the development of nephrocalcinosis does not always require hypercalciuria, but alterations in urinary inhibitors of crystal formation (e.g. citrate, magnesium), urinary excretion of oxalate and urine pH may also play a role [1,8]. The possibility of nephrocalcinosis being due to type I renal tubular acidosis must be excluded by a complete nephrologic examination (serum potassium, pH, bicarbonate, tubular acidification test with NH_4Cl).

Our findings are consistent to previous reports suspecting long-term furosemide treatment in adults may cause mild medullary nephrocalcinosis, characterized by peripheral deposition of calcium salts in the pyramids with depressed renal function. In nephrocalcinosis, ultrasound examination shows an increase in medullary echogenicitiy which can be massive or appear only as an echogenic ring at the periphery of the renal pyramids [9]. This pattern is an early manifestation of nephrocalcinosis [10]. This could be useful information to sonographers involved in the diagnosis of nephropathy. CT is the most accurate and sensitive technique and therefore the modality of choice [2]. In conclusion, we considered that furosemide treatment should be part of differential diagnosis list of medullary nephrocalcinosis in adults undergoing long-term therapy with this drug, especially if the high dose of drug is used as in this case.

References

1. Alon US. Nephrocalcinosis. Curr Opin Pediatr. 1997; 9: 160-165.
2. Kim YG, Kim B, Kim MK, Chung SJ, Han HJ, Ryu JA, et al. Medullary nephrocalcinosis associated with long-term furosemide abuse in adults. Nephrol Dial Transplant. 2001; 16: 2303-2309.
3. Hufnagle KG, Khan SN, Penn D, Cacciarelli A, Williams P. Renal calcifications: a complication of long-term furosemide therapy in preterm infants. Pediatrics. 1982; 70:360-363.
4. Jacobs TP, Bilezikian JP. Clinical review: Rare causes of hypercalcemia. J Clin Endocrinol Metab. 2005; 90: 6316-6322.
5. McGuinness B, Logan JI. Milk alkali syndrome. Ulster Med J. 2002; 71: 132-135.
6. Garel L, Filiatrault D, Robitaille P. Nephrocalcinosis in Bartter's syndrome. Pediatr Nephrol. 1988; 2: 315-317.
7. Herlitz LC, Bruno R, Radhakrishnan J, Markowitz GS. A case of nephrocalcinosis. Kidney Int. 2009; 75: 856-859.
8. Wardener HE. Idiopathic edema: role of diuretic abuse. Kidney Int. 1981; 19: 881-891.
9. Simoes A, Domingos F, Prata MM. Nephrocalcinosis induced by furosemide in an adult patient with incomplete renal tubular acidosis. Nephrol Dial Transplant. 2001; 16: 1073-10744.
10. al-Murrani B, Cosgrove DO, Svensson WE, Blaszczyk M. Echogenic rings--an ultrasound sign of early nephrocalcinosis. Clin Radiol. 1991; 44: 49-51.