Renal Oxalosis in a Calf

M. Yavuz GÜLBAHAR
Yüzüncü Yıl University, Faculty of Veterinary Medicine, Department of Pathology, 65080, Van - TURKEY

Abdullah KAYA
Yüzüncü Yıl University, Faculty of Veterinary Medicine, Department of Internal Medicine, 65080, Van - TURKEY

İsmail GÖLEN
Yüzüncü Yıl University, Faculty of Veterinary Medicine, Department of Pathology, 65080, Van - TURKEY

Abstract: A case of neonatal renal oxalosis in a 7-day-old calf is described. Clinical biochemistry revealed increased blood urea nitrogen. Gross findings included thin renal medulla and dilated renal calyces containing numerous, small, pale yellow and granular calculi. Histologically, most cortical and medullary tubules were dilated with birefringent crystals, whereas the glomeruli appeared unaffected. The crystals were morphologically consistent with calcium oxalate by the Pizzolato technique. Diffuse interstitial fibrosis and focal accumulations of lymphocytes were also noted.

Key Words: Calf, hyperoxaluria, renal oxalosis

Bir Buzağıda Renal Okzalozis Olgusu

Özet: Çalışmada 7 günlük bir buzağıda renal okzalozis tanımlandı. Biyokimyasal analizlerde kan üre nitrogen düzeyinin yüksek olduğu belirlendi. Makroskobik olarak, buzağının böbrek medullası incelmişti ve genişlemiş renal kalikslerde çok sayıda, küçük, açık sarı renkte ve granüler görünümde taşlar mevcuttu. Histolojik incelemede, çoğu kortikal ve medullar tubulusların ışığı kıran kristaller nedeniyle genişlediği dikkati çekti. Buna karşın glomeruluslarda bozukluğa rastlanmadı. Kristallerin morfolojik olarak Pizzolato tekniği ile yapılan boyamalarında kalsiyum okzalat kristalleri oldukları belirlendi. Ayrıca interstisyel fibrosis ve fokal lenfosit infiltrasyonları mevcuttu.

Anahtar Sözcükler: Buzağı, hiperokzaluri, renal okzalozis

Introduction

Renal oxalosis occurs after the deposition of calcium oxalate crystals in normal tubules. The crystal deposition is primarily within the proximal convoluted tubules and results in end-stage renal disease characterized by renal atrophy and interstitial fibrosis (1-6). Renal oxalate crystals have been observed in calves with (1) or without (5) congenital anomalies, and in lambs from a flock fed moldy feed (7), and have been experimentally induced in ovine fetuses by feeding their dams oxalic acid (8). Renal oxalosis, caused by ingestion of ethylene glycol, has been reported in a Jersey calf and experimentally induced in cattle (9). In ruminants, renal oxalosis is usually associated with ingestion of oxalate-containing plants (6,10-12). Neonatal oxalate nephropathy is a rare condition in calves and to our knowledge there has been no case associated with neonatal oxalosis in Turkey reported in the literature. The present case describes neonatal nephropathy, a rare condition, in a native calf.

Materials and Methods

The calf, a 7-day-old female, was from a native cow in Van in eastern Turkey. The owner stated that the dam was grazed on natural pasture and was fed wheat straw with concentrate feed. This calf was the third purebred native offspring of the dam from natural insemination with the same native bull. There was no history of the same illness associated with the dam and bull or other offspring. The calf exhibited lethargy, severe muscular weakness, and recurrent, greenish diarrhea after the fourth day of life. The calf was admitted to the Animal Hospital in Yüzüncü Yıl University for evaluation when it was seven days old. Despite being treated with antibacterial agents, vitamins and fluids that contained electrolytes, the calf died within 15 minutes of admission. Blood samples from the calf were obtained and the glucose, blood urea nitrogen (BUN), serum creatinine (SC), creatinine kinase (CK), alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine

aminotransferase (ALT), lactate dehydrogenase (LDH), gamma-glutamyltransferase (GGT), total protein, albumin, calcium and phosphorus were examined. The examination of urine was not possible.

The calf was necropsied and tissue samples fixed in 10% neutral formalin were processed routinely, embedded in paraffin, sectioned at 5 µm and stained with hematoxylin and eosin (H&E), Pizzolato, periodic acid-Schiff and Masson's trichrome stains.

Results

Physical examination revealed severe dehydration, marked weakness, and pale mucous membranes. The calf was thin and its hindquarters were dirty with feces.

Gross lesions were limited to the kidneys, which were pale and soft. On the cut surface, renal medullas were thin and some renal calyces were dilated and contained numerous, small, pale yellow, granular calculi (Fig. 1). Histopathologically, most cortical and medullary tubules were greatly dilated with birefringent crystalline casts, whereas glomeruli appeared unaffected (Fig. 2). The crystals were morphologically consistent with calcium oxalate crystals and stained for calcium oxalate by Pizzolato's technique (Fig. 3). The affected tubular epithelium was finely vacuolated and often degenerated. The cytoplasm of a few tubular epithelia contained birefringent crystals. Mild to moderate, focal tubular

epithelial hyperplasia was noted. Some tubules, especially those in the medulla, contained PAS-positive hyaline casts that were admixed with calcium oxalate crystals, degenerated cellular debris and a few inflammatory cells (Fig. 4). Numerous birefringent crystalline deposits were scattered in the interstitium. Diffuse, interstitial fibrosis and small, focal accumulations of lymphocytes were noted in the renal cortex and to a lesser extent in the medulla (Figs. 2 and 4).

Discussion

Pathological findings and increased urea level were consistent with the end-stage renal disease. BUN and SC are used exclusively as indices of retention of nitrogenous wastes by the kidney. However, in humans, it is reported that BUN correlates more directly with symptoms of uremia than SC (13). In the present case, clinical chemistry revealed increased BUN while SC level showed no change compared with reference values (14). Moreover, animals may not have elevated BUN and SC values despite the existence of renal dysfunction. In contrast, abnormally high BUN and SC values may be found in patients with normal renal function (13). The nephrotoxicity of oxalates involves more than mechanical obstruction and may be due to in part to intracellular chelation of calcium and magnesium and hence interference with oxidative phosphorylation (6).
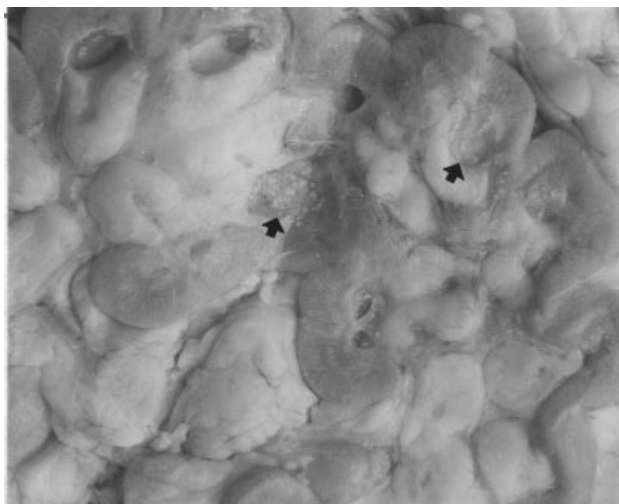

Figure 1.   Gross appearance of the kidney. Note the dilated calyces containing granular oxalate calculi (arrows).
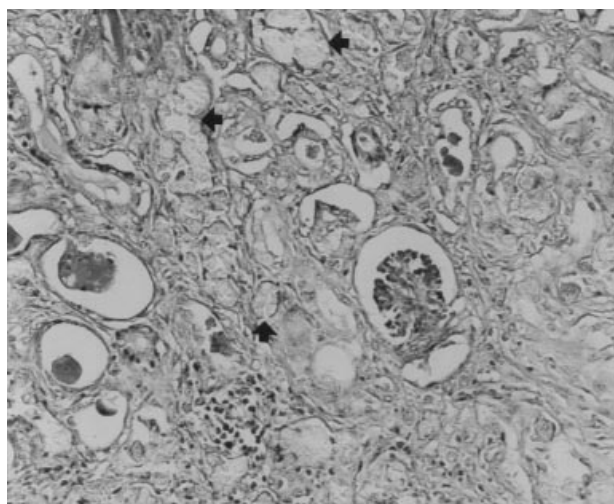

Figure 2.   Focal lymphocytes accumulation and extensive interstitial fibrosis separating degenerated tubules with calcium oxalate crystals (arrows) in the cortex. H&E, x200.
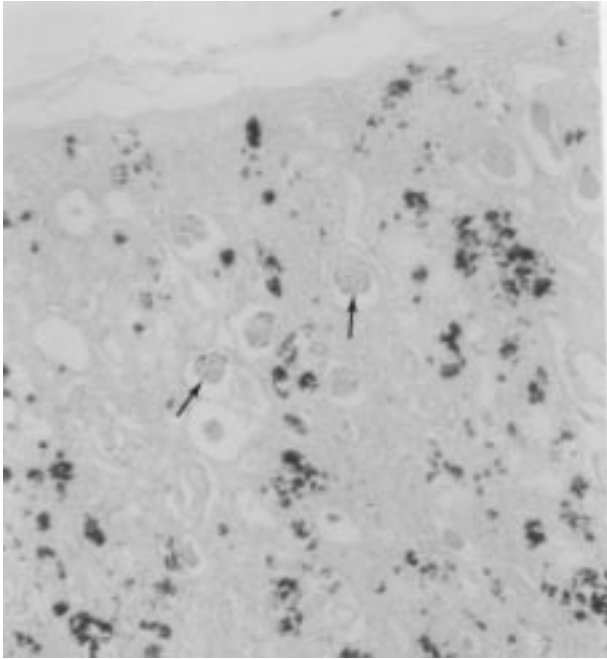
Figure 3.   Calcium oxalate crystals stained black with the Pizzolato technique in the cortex. Note the unstained glomeruli (arrows). Pizzolato stain, x80.
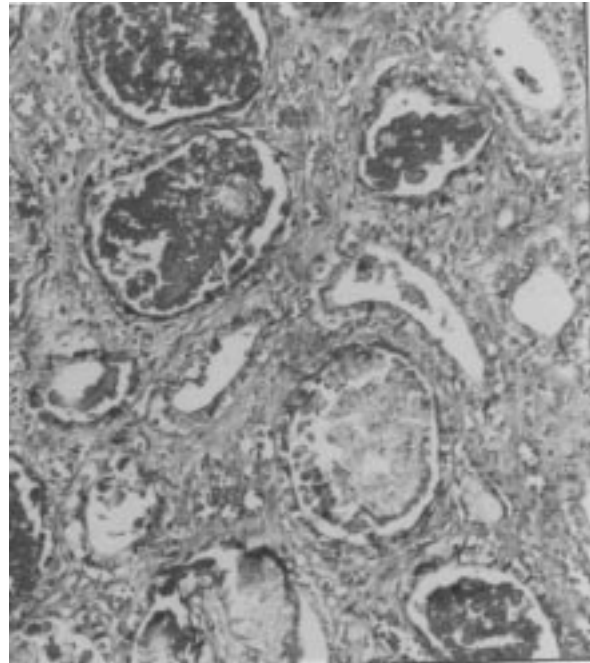

Figure 4.   Interstitial fibrosis and hyaline droplets admixed calcium oxalate crystals in the medullary tubules. H&E, x200.

In humans, the condition is well defined and is caused by either a congenital enzyme deficiency (primary hyperoxaluria) or by endogenous or exogenous poisoning (secondary hyperoxaluria). Primary hyperoxaluria is used as a general term for rare genetic disorders of the glyoxylate metabolism (15). The disease has been associated with offspring of consanguineous marriages in small and relatively isolated communities (16). The most common form of primary hyperoxaluria, type I, is inherited as an autosomal recessive trait and there is an inborn deficiency of the liver peroxisomal enzyme alanine:glyoxylate aminotransferase (AGT). Type II is an inborn deficiency of D-glycerate dehydrogenase, and a recently defined form, type III, is an idiopathic form and is associated with intestinal hyperabsorption of oxalate in the absence of any of the recognized gastro-intestinal diseases that increase oxalate absorption (15,16). In animals, the condition resembling primary hyperoxaluria in humans has been described in Tibetan Spaniel pups as type I (4) and in cats as type II (2). However, in ruminants, this condition has not been well defined.

Secondary hyperoxaluria may develop as a consequence of excessive dietary intake of oxalate-containing feed, such as rhubarb, spinach, chocolate, tea or from poisoning with certain chemical substances, such as ethylene glycol, which are metabolized to glycolic acid, glyoxylate and oxalate (6,9). Pyridoxine deficiency, large doses of ascorbic acid (vitamin C), anesthesia with methoxyfluorane or aspergillus infection may also lead to secondary hyperoxaluria (6,15). In ruminants, oxalate poisoning caused by some oxalate-producing plants such as *Rumex* spp., *Halogeton glomeratus* or grasses of the genera *Cenchrus, Panicum* and *Setaria* have been reported (6,10-12). The presence of kidneys containing oxalate crystals was reported in fetuses in which no etiological cause of abortion was detected (17,18). The finding of oxalate crystals in the kidneys of lambs from sheep fed oxalate-containing feed suggests that oxalic acid can cross the placental barrier (8). However, a few oxalate crystals can frequently be found in scarred tubules in any species; these crystals are usually without significance and do not cause mortality in animals (6).

The gross and microscopical findings seen in the kidneys of this calf were similar to changes seen in other animal cases (1,2,4,5,7,8,12) and in humans with primary hyperoxaluria (15,16,19). The extra renal deposition of calcium oxalate crystals has been reported in animals with oxalosis (5) and is common in humans

with primary hyperoxaluria (15,16). In the present case, extra renal deposition of calcium oxalate crystals was not seen in the other organs examined. The detailed history of the calf suggested that there had been no exposure to agents that could have produced secondary hyperoxaluria and there was no close familial relation between the parents, and so it is impossible to explain the reason for the oxalate nephropathy exactly. More studies including the analysis of enzymes in frozen tissue specimens, in particular the liver, are needed to further define mechanisms involved in bovine renal oxalosis.

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