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ALL THAT GLITTERS IS NOT GOLD – THE UTILITY OF A RENAL BIOPSY IN DIAGNOSIS

Keren Cohen-Hagai[1], Ze'ev Korzets[1,3*], Eleonora Plotkin[1,3] ,Tanya Zahavi[2,3], Sydney Benchetrit[1,3]

[1]Departments of Nephrology and Hypertension, Meir Hospital, Kfar-Saba Tel-Aviv University, Ramat Aviv, Israel Meir Hospital, Sapir Medical Center Kfar - Saba, 4425009 Israel.
[2]Departments of Pathology , Meir Hospital, Kfar-Saba Tel-Aviv University, Ramat Aviv, Israel Meir Hospital, Sapir Medical Center Kfar - Saba, 4425009 Israel.
[3]Sackler School of Medicine, Tel-Aviv University, Ramat Aviv, Israel Meir Hospital, Sapir Medical Center Kfar - Saba, 4425009 Israel.

Corresponding Author:- **Ze'ev Korzets**
E-mail: korzets.zeev@gmail.com

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ABSTRACT
The estimated incidence of acute kidney injury (AKI) is between 2-3 cases/1000 persons. Disturbingly, in a recent report only 50% of patients with AKI received good medical care. Establishing the cause of the AKI is therefore paramount to ensure correct management. Often, the etiology is obscure due to the presence of multiple predisposing factors. We present a case of rapidly progressive AKI in a young male patient who had a background of a solitary kidney, systemic mastocytosis, hepatitis B carrier status and alcohol abuse. Ultimately, this patient's diagnosis was determined by renal biopsy.

PATIENT DESCRIPTION

21 year old Caucasian male presented to the emergency room (ER) with left flank pain. He had been previously diagnosed as suffering from systemic mastocytosis following several episodes of anaphylaxis, elevated serum tryptase levels and a skin biopsy. He currently receives no medication for this condition. The patient is also known to have agenesis of his right kidney and is a hepatitis B carrier. He is a heavy smoker (10 pack years) and admits to an alcoholic intake of half a bottle of vodka per day. Prior to being seen in the ER, he had been administered NSAID's (diclofenac) with some relief of his pain. There is no documented history of previous renal colic or nephrolithiasis.

On examination, he appeared quite at ease, weight 110 Kg, height 1.85 m ,temperature 36.6^0 C, pulse 58/min and regular, blood pressure 160/95 mmHg. Apart from mild tenderness over his left flank, the remainder of the physical examination was unremarkable.

Initial laboratory data showed WBC count 8380/ L, Hb 14.3 g/dl, platelets 184,000 / L, Na 134mEq/L, K 4.7 mEq/L, glucose 125 mg/dl. Serum creatinine was 3.5 mg/dl (last recorded value 0.81 mg/dl 14 months ago), urea 65 mg/dl, Ca 11.4 mg/dl with a serum albumin of 3.5 g/dl, Pi 3.0 mg/dl and PTH 182 pg/ml. On dipstick urinalysis there were RBC 80/ L and proteinuria >300 mg/dl. Urine sediment showed numerous RBC/HPF, several leucocyte and hyaline casts and no crystals.

Arterial blood gases: pH 7.34, HCO_3 18.3 mEq/L, pCO_2 34.3 mmHg.

A non- contrast abdominal computed tomography revealed a hypertrophied left kidney with no hydronephrosis and no evidence of renal calculi. Bilateral inguinal and left sided retroperitoneal lymph nodes were enlarged. Chest X-ray was normal except from a slightly enlarged mediastinum.

On admission, the patient was administered intravenous saline. Despite this, serum creatinine continued to increase reaching 8.4 mg/dl on day 5 of hospitalization. A serological survey showed ANA, complement levels, ANCA, anti-GBM antibodies, angiotensin converting enzyme to be either negative or within normal limits. HBsAg was positive as was HBcAb. HBsAb and HBeAg were negative. Quantitative HBV-PCR was 13,290 IU/ml. HCV antibodies were negative. Protein electrophoresis was normal. In view of the rapidly progressive renal failure, the patient was treated with intravenous pulse steroids under coverage of lamivudine.

Percutaneous ultrasound guided renal biopsy was performed. On light microscopy, there were 9 glomeruli showing only mild mesangial proliferation. Proximal tubules showed hyaline droplet changes, flattened epithelia with a widened lumen and apical blebbing. Distal tubules were seen to contain crystalloid structures which under polarized light were brilliantly birefringent (Fig. 1,2). Several tubules showed signs of regeneration as evidenced by mitoses in the tubular epithelia. There were no mast cell or any other interstitial cellular infiltrates.

Questions

What is your diagnosis?

Would an anion gap and an osmolar gap been useful in diagnosis?

ANSWER AND COMMENT (DISCUSSION)

This patient with a solitary kidney presented with left flank pain and rapidly deteriorating renal function. Imaging studies did not reveal any nephrolithiasis or obstructive uropathy. The differential diagnosis of the acute kidney injury prior to the biopsy was wide and included both glomerular and tubulointerstitial disease. Possible glomerular injury was rapidly progressive glomerulonephritis either secondary to HBV infection or anti-GBM disease despite the absence of anti GBM antibodies. It was this consideration which led to the being "blindly" administered intravenous pulse steroids. Possible tubulointerstitial disease included that secondary to systemic mastocytosis, NSAID induced injury and sarcoidosis, the latter considered because of a widened mediastinum and hypercalcemia.

Renal biopsy was essential in making the correct diagnosis. The performance of a percutaneous renal biopsy of a solitary kidney was, once, considered an absolute contraindication. Technical and real time imaging improvements over the last decades have, however, made this procedure entirely feasible with a low complication rate [1-4].

Our patient's biopsy showed acute tubular necrosis (ATN) associated with the intratubular deposition of crystals whose appearance and refringence under polarized light were characteristic of calcium oxalate. The established diagnosis was, therefore, calcium oxalate induced renal injury. This finding led us to take a more detailed anamnesis. Upon directed questioning, the patient, a chronic alcohol abuser, admitted to having drunk an unknown quantity of a home made alcoholic mixture consisting of ethanol and ethylene glycol, three days before presenting in the ER.

Ethylene glycol (EG) intoxication is typically divided into three stages [5]. The first stage (30 minutes to 12 hours post ingestion) is manifested by central nervous system depression, hyperosmolality and gastrointestinal upset. Our patient did report a short period of disorientation following his binge but attributed it to his inebriated state.

The second stage (12-24 hours after ingestion) is dominated by metabolic acidosis and associated cardiopulmonary symptoms (tachypnea, , tachycardia, pulmonary edema and /or cardiac failure. Often, the cardiopulmonary effects are either minor or not evident.

The third stage (24-72 hours after ingestion) is characterized by flank pain and the onset of oliguric/anuric ATN due to calcium oxalate deposition. This clinical scenario is identical to that of our patient who presented 72 hours after ingestion.

Toxicity and clinical symptomatology of EG poisoning are due to the accumulation of its metabolites. The clinical picture is, therefore, dependent on the time of ingestion and time of presentation after the acute exposure. EG intoxication has, classically, been described as giving rise to a combination of an osmolar gap and a high anion gap metabolic acidosis. The parent compound accounts for the osmolar gap whereas glycolic acid is the metabolite most responsible for the high anion gap metabolic acidosis. Neither an anion gap or osmolar gap were evaluated in our patient. However, as alluded to above, with the delay in presentation it is reasonable to assume that the osmolar gap of our patient will have resolved as elsewhere described [6,7] . Furthermore, our patient showed only a mild metabolic acidosis (pH 7.34 with a base excess of -6.1 mEq/L). This is in contrast to the case series of EG and methanol poisonings reported by Montjoy *et al.*, [8] in which the mean pH was 7.02 with a mean anion gap of 21 mEq/L. This discrepancy probably resulted from either a low amount of ingested toxin or, more importantly, the concomitant consumption of ethanol as was the case in our patient and the delayed presentation. Ethanol is a known powerful competitive inhibitor of alcohol dehydrogenase. Albeit, ongoing metabolism of glycolic acid resulted in the accumulation of the end product of EG, namely oxalic acid and eventual deposition of calcium oxalate crystals in the kidney. Calcium oxalate crystalluria would, no doubt, have

pointed us in the right direction. However,in keeping with the literature in which only 50% of patients exhibit this hallmark of EG poisoning [5], it was not found in our case.

The renal toxicity of EG has been suggested as due to its aldehyde metabolites, glycoaldehyde and glyoxalate. Recent evidence, however, has shown that it is rather the calcium oxalate crystals which produce the renal damage [9,10], The severity of renal damage in EG dosed rats correlates with the total accumulation of calcium oxalate in kidney tissue. The mechanisms involved include a combination of altered membrane function and structure, the production of reactive oxygen species radicals and mitochondrial dysfunction.

Fig 1. Light microscopy showing intratubular (distal tubule) crystalloid structure (H&E)

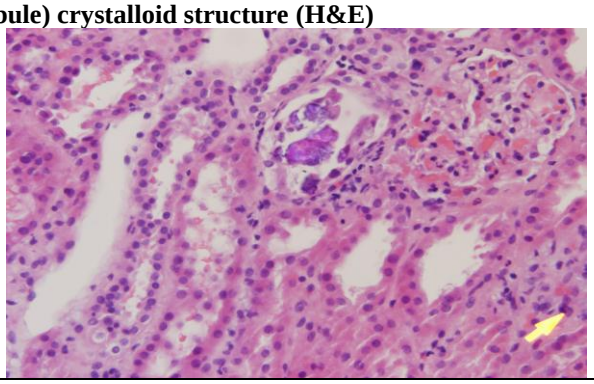
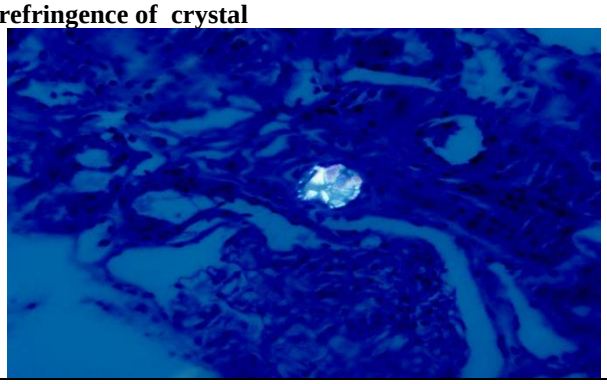


Fig 2. Polarized light microscopy showing brilliant birefringence of crystal



CONCLUSIONS

The case presented serves to highlight several issues:

1. In a chronic alcohol abuser, unexplained AKI should always alert the physician to the possibility of EG or other alcohol poisoning. A high index of suspicion is mandatory.
2. A solitary kidney should not be a deterrent to percutaneous renal biopsy
3. Depending on the time of presentation after ingestion, EG intoxication can present "atypically" that is, lacking the characteristic laboratory abnormalities such as an osmolar gap and a marked high anion gap metabolic acidosis.

CLINICAL FOLLOW UP

Kidney function returned to normal within 2 weeks.

CONFLICT OF INTEREST

None declared

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