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Case Reports

Drug Induced Acute Interstitial Nephritis

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SUMMARY

Acute interstitial nephritis induced by drugs is an under-estimated and under-reported disease entity. We present 3 cases with an abrupt decline in renal function following the use of antibiotics. Two patients presented with oliguria while in the third patient no oliguria was noted. One patient required dialysis during the acute phase. Diagnosis of acute interstitial nephritis was confirmed by presence of a heavy interstitial infiltrate on kidney biopsies. All three responded very well to discontamination of antibiotics. We conclude that a high degree of suspicion is required to clinch the diagnosis of acute interstitial nephritis and stopping the offending drug in time leads to complete recovery.

INTRODUCTION

Acute Renal Failure (ARF) is a syndrome characterized by a relatively abrupt decline in renal function that leads to the accumulation of water, crystalloid solutes and nitrogenous metabolites in the body. Clinically significant acute renal failure is usually associated with a daily increase in the serum creatinine and urea nitrogen levels greater than 0.5 and 10 mg/dl respectively. It may be prepenal (e.g. hypovolumia), postrenal (e.g. Ureteral obstruction) or renal. Renal causes may include pathology of any of the major elements of kidney i.e. blood vessels (vasculities), glomerulus (Clomerulonephritis), Tubules (Acute Tubular Necrosis) or Interstitium (Acute Interstitial Nephritis). Here we are presenting three cases of Acute Interstitial Nephritis, that developed after taking drugs.

Presentation

A 40 years old male presented on 17-4-1992 with complaints of fever 9 days moderate to high grade, sometimes associated with rigors. On the 2nd day of fever he was put on "Amoxil". Oliguria, Progressing to Anuria occurred 6 days later. This was accompanied by periorbital and leg swelling. On initial examination, temperature, 100°F, B.P. 130/85 mm of Hg, pallor, -ve; oedema, +ve (Periorbital and both legs) No Lymphadenopathy Examination of abdomen, chest cardiovascular system and central nervous system revealed no abnormality.

Initial Laboratory, Date 17-04-1992

Urea, 79 mg/dl; Creatinine, 5.7 mg/dl; serum Na+, 133 mmol/l; Serum K+, 3.5 mmol/l; Hb, 12.3 g/dl; TLC, 10.9×10^9/; DLC polys, 53%; Lympho, 43%, EOS, 04%.

T. bilirubin, 0.4 mg/dl; D bilirubin, 0.2 mg/dl; SGPT, iu/l (normal upto 40 iu/l); SGPT, 16 iu/l (normal upto 40 iu/l); Urine proteins, traces; Urine PHS cells, 4-5/HPF. Urine RBCS, Nil; Widal test, -ve; ANA, -ve; RA factor, -ve; ASO titter, 200.0 iu/ml (normal upto 200 iu/ml); C_3, 72.0 mg/dl (normal = 55-120) C_4, 35.0 mg/dl) normal = 20-50).

Clinical Follow-up

A) Temperature

Very around 99°F - 103°F but after 25-04-1992, tended to decline, and then settled, without any antibiotics.

B) Urine Out PHT

Increased from 50 cc on 17-04-1992 to 1300 cc on 30-04-1992.

Laboratory Follow-up 18-04-1992

Urea, 127 mg/dl; Creatinine, 7.3 mg/dl, 20-4-92 Urea, 205 mg/dl; creatinine, 10.0 mg/dl, 24-4-92; Urea, 65 mg/dl, Creatinine, 2.0 mg/dl; Hb, 12.3 g/dl; TLC, 11.0×10^9/l; DLC Poly, 53%; lymph, 07%; EOS,

07%; Mono, 02%. 01-05-92 urea, 30 mg/dl, creatinine, 1.0 mg/dl.

Renal Biopsy

Carried out on 23-04-92, showed 11 glomeruli - all normal with dense interstitial infiltrate containing lymphocytes, eosinophils, giant cells and epithelioid granolomas.

Renal Diagnosis

The pattern of rise of urea and creatinine and then recovery, puts this case into acute renal failure syndrome. The history of antibiotic (Amoxicillin) intake, Eosinophilia and biopsy report, show that the cause is acute interstitial nephritis.

Case No. 2

A 55 years old male was admitted to the nephrology ward with two weeks history of breathlessness and vomiting four weeks age. he was diagnosed by a local doctor to have diabetes mellitis, hypertension and U.T.I., and was prescribed Captopril and Tarivid.

On examination he was dyspnoeic, B.P. 160/100 pericardial rub +ve.

Urine output 1800 ml/day.

Blood urea, 220 mg/dl serum creatinine, 8.0 mg/dl. He was dialysed and renal biopsy done, that showed acute interstitial nephritis. Kidney function gradually improved.

Case No. 3

A 45 years old male was admitted to surgical ward with one month history of pain in right hypochondrium and jaundice. Examination revealed jaundice, fever and tender hypochonodrium. A clinical diagnosis of obstructive jaundice due to cholangitis was made and he was put on pipericillin 2 gram I.V., three times a day. His abdominal u/s showed small ealculi in gall bladder, CBD, 0.9 cm and mild intrahepatic, 10 mg/dl and creatinine, 0.6 mg/dl; urine analysis was normal.

During next five days fever subsided, but urine output reduced to 100 ml/day. Repeat urine showed traces proteins and sp. gravity, 1012. Serum urea and creatinine gradually rose to 178 mg/dl and 8.0 mg/dl respectively. An initial diagnosis of ARF due to A.T.N. or AIN was made. Biopsy showed findings consistent with AIN.

Pipercillin was stopped and he was managed conservatively. He improved in next few days. His urine output reached more than 1000 cc/day. On discharged urea, 60 mg/dl, creatinine, 1.8 mg/dl.

DISCUSSION

Acute interstitial Nephritis (AIN) is characterized by the association of acute renal failure and infiltration of renal interstitium by inflammatory cells[1].

Table 1: Main causes of acute interstitial nephritis.

A) DRUG INDUCED

B) INFECTIONS
Septicemia
Leptospirosis
Hemorrhagic Fever
Diphtheria, scarlet fever, streptococcal infections, penumococcal infections, toxoplasmosis, typhoid fever, infectious mononucleosis, measles, brucellosis, syphilis, Mycoplasma pneumonine, Rocky Mountain spotted fever, Legionnaires disease.

C) MALIGNANT CELL INFILTRATION
Myeloma, Lymphomas, acute leukemias[5]

D) SYSTEMIC DISEASES
Systemic lupus erythematosus[7], sarcoidosis, Sjogren's syndrome.

E) IDIOPATHIC
Wieth uveitis
Isolated
Megalocytic interstitial nephritis.

Table 2: Incidence of acute interstitial nephritis (AIN) in patients with acute renal failure (ARF)

	Total No. of with ARF	*Patients with renal biopsy*		
			No.	*%*
Richet et al.[16]	976	218	8	0.8
Linton et al.[17]	108		9	8.3
French Cooperative study 1984	2175	77	17	0.8

The main causes of AIN are listed in Table 1. It is currently stated that drug, induced AIN

predominates. The real incidence of AIN is unknown, few studies are shown in Table 2. But the real incidence may have been underestimated in these, because its incidence is unknown in ARF patients who did not undergo renal biopsy. Table 3 shows drugs that are associated with AIN. Table 4 shows some clinical features of AIN associated with penicillins. The mainstay of therapy is to discontinue the responsible drug or to treat the inciting infection. Renal function will improve in most patients. The role of steroids is uncertain. They may hasten the recovery and may cause more complete recovery.

Table 3: Drugs association with acute interstitial nephritis

Strong Association	*Probable association*	*Weak association*
Methicillin[1]	Carbenicillin	Phenytoin
Penicillins	Cephalosporins	Tetracycline
Cephalothin[9]	Oxacillin	Probenecid
Nonsteroidal anti-inflammatory[3] drugs cimetidine[11]	Ampicillin	Captopril[14]
	Sulfonamides	Allopurinol
	Rifampin	Erythromycin
	Thiazides[10]	Chloramphenicol
	Furosemide[10]	Clotibrate[6]
	Leukocyte interferom	
	Phenindione	

Table 4: Acute interstitial nephritis associated with B-lactam antibiotics. Main clinical and pathologic features

1. Time of development ranges from 2 to 60 days.
2. Fever, skin rash, hematuria, blood eosinophilia and or eosinophiluria are common.
3. Nonoliguric renal failure with mild proteinuria is frequent.
4. Renal biopsy shows interstitial infiltrates composed of lymphocytes, often eosinophils, sometimes epithelial cell granulomas.
5. Circulating anti TBM antibodies are inconstantly found.
6. Renal recovery is usual after withdrawal of the offending drug. Steroid therapy seems effective in some cases.

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