

Unusual case presentation of Ertapenem induced Acute Interstitial Nephritis (AIN) in a case of Protein S deficiency and factor V Leiden mutation with Deep Vein Thrombosis

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Abstract: Interstitial nephritis is a usually short-term disorder. In rare cases, it can cause permanent damage, including chronic kidney failure. Acute interstitial nephritis may be more severe and more likely to lead to long-term or permanent kidney damage in elderly people, if not diagnosed early. Acute Interstitial Nephritis (AIN) is known to occur following analgesics and certain antibiotics. We present a case of 58 years old male patient, who presented with high fever for which injection Ertapenem was started empirically at Dubai hospital. Patient was a known case of Deep Vein thrombosis of left leg since 5 years on warfarin therapy. Patient came to India for high fever and further management. Patient developed proteinuria with high creatinine and urinary abnormalities. Renal biopsy revealed Acute interstitial Nephritis (AIN). In addition, he was diagnosed to have Protein S deficiency with Factor V Leiden mutation.

Key words: High fever, Creatinine, Proteinuria, Renal biopsy, Antibiotics, Deep vein thrombosis, Protein S deficiency, Factor V Leiden mutation

58 years old male patient presented with history of high fever which was continuous in nature and

without chills for six days. He did not give any history of urinary disturbance or frequency of urine. No

history of abdominal pain, loose motion or vomiting. No history of cough, chest pain or breathlessness.

Patient was in Dubai where he got admitted to the hospital for the same. He is a non smoker, non-

alcoholic, having hypertension since last ten years on Tab. Telmisartan 40 mg, Tab. Indapamide and Tab.

Lercanidepin 10 mg once a day. He gave history of DVT of left leg (detected on venous Doppler) 5 years

ago and presumed to be idiopathic and started on Tab. Warfarin 5 mg OD. Patient had received Inj.

Ertapenem 1 gm IV BD for four days. Along with this antibiotic, patient received paracetamol, vitamins

and Intravenous fluids. Patient took transfer from Dubai hospital to Mumbai as there was no

improvement in fever. On examination, he was afebrile, haemodynamically stable, minimal oedema

feet, JVP not raised, no basal crepitations or rhonchi present.

Investigations revealed were as follow:

Hb 10 gm/dL WBC 7520/cu.mm (N 63%/ L 26%/ E 4%/M 7%), Platelet count 3,91,000/cu.mm Rapid

malarial test : Negative, Peripheral Smear for Malaria parasite: Negative, Widal test : Negative, CRP 3.3

mg/dL, FBS: 96 mg/dl, BUN 33.6 mg/dL, Creatinine 3.0 mg/dL, Uric acid 9.4 mg/dL, Calcium 8.2 mg/dL

Phosphorous: 5.7 mg/dL, Proteins: 5.3 gm/dL, Albumin 2.0 gm/dL Sodium: 138 mEq/L, Potassium 4.8

mEq/L, Chloride: 106 mEq/L, SGPT 128 U/L, Alkaline phosphatase: 100 U/L, Bilirubin 0.5 mg/dL, Urine

Protein: 3 plus, RBC 8-10/hpf, leucocytes 2-4/hpf, 24 hours urine for protein: 392 mg/24 hours, Urine

routine examination did not revealed eosinophils, HCV Igm antibody- negative, HbSAg –negative and

HIV negative. USG (Abdomen and pelvis) Revealed: Both kidneys are normal size and shape. Both

kidneys shows increased cortical echogenicity suggestive of medical renal disease, Chest X ray: Normal

, Urine Culture: Negative, Blood culture: Negative, Renal color Doppler: Does not show changes of

significant renal artery stenosis, ANA 1:80 titre, C-ANCA and P-ANCA: Negative, C3, C4 complements

were normal, Protein C 85% (67%-195%) Normal, Protein S 40% (77%-143%) low. Antithrombin activity

90% (70%-122%) Normal, Factor V leiden mutation detected, APLA IgG 3.1 U/mL(normal), APLA IgM 3.0

U/MI(normal), BT: 2 min 45 sec, CT: 6 min 55 sec, INR 1.0. Exact cause of fever could not be

ascertained. Fever subsided within a week with conservative treatment and it was self limiting, but

proteinuria and azotemia continued. In view of abnormal urine picture and high creatinine, renal

biopsy was taken after stopping Tab. Uniwarfarin. However patient developed frank hematuria

followed by clot inside the urinary bladder which required evacuation under anesthesia. Renal biopsy

revealed five glomeruli are seen. All are reported normal. The arterioles are thick and hyalinized.

Significant patches of inflammatory cells viz lymphocytes, monocytes, plasma cells and few

eosinophils in the interstitium are seen. Immunofluorescence study revealed IgG, IgM, IgA, C3, C1q

and fibrinogen are all negative. After diagnosing Interstitial nephritis on biopsy, Tab Prednisolone 40

mg per day was started. Creatinine started reducing to 2.4 and 1.8 after 10 days of steroid therapy and

over period of 6 weeks. Creatinine came to near normal with tapering dose of steroids. Patient was

advised to keep PT/INR between between 2 to 3 with Tab. Uniwarfarin 5 mg once a day.

Discussion:

Antibiotics are powerful agents with the potential for great clinical benefits in the treatment of

Infectious diseases, however they are not benign and may cause significant adverse reactions like Acute

Interstitial Nephritis (AIN). (1) AIN is an uncommon form of acute renal failure that is usually

medication related. Although the clinical features and renal histopathology are well recognized,

therapy beyond discontinuing the offending drug has been a challenge (2). Classic findings of fever, rash

and arthralgias may be absent in upto two thirds of patients (3). Diagnostic studies such as urine

eosinophils and renal gallium 67 scanning provide suggestive evidence, but they are unable to reliably

confirm or exclude the diagnosis of acute interstitial nephritis (4),(5). Renal biopsy remains the gold

standard for diagnosis, but it may not be required in mild cases or when Clinical improvement is rapid

after removal of an offending agent or medication. (6) The time until removal of such agents, and renal

biopsy findings, provide the best prognostic information for return to baseline renal function

(7). Corticosteroids appear to provide some benefit in terms of clinical improvement and return of renal

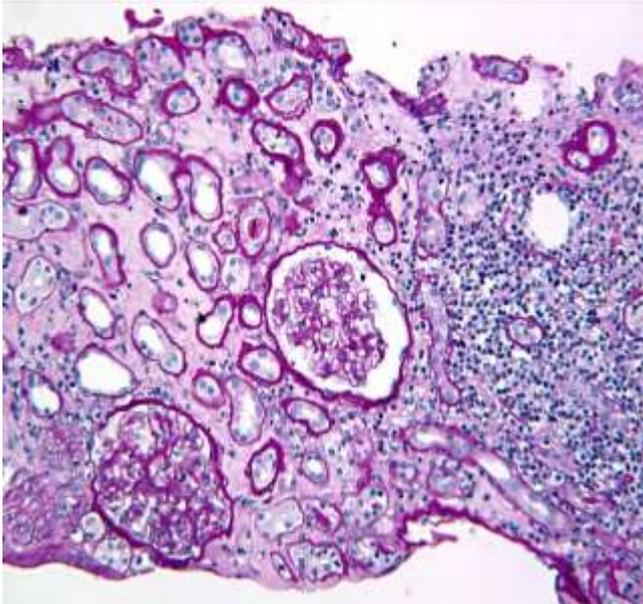
function, but no controlled clinical trials have been conducted to confirm this (8). In our patient, after

renal biopsy steroid started and creatinine level after 3 weeks started falling and became 1.8 mg% and

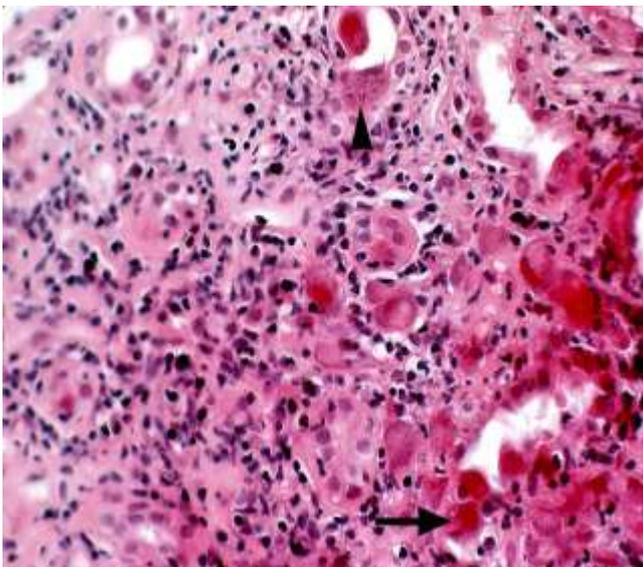
remained static. Patient clinically and symptomatically improved. Ertapenem induced interstitial

nephritis has not been reported in literature. Our patient, in addition also has factor V leiden

mutation with Protein C deficiency with deep vein thrombosis in leg.



Picture 1: Interstitial nephritis



Picture 2: Interstitial Nephritis

References

1. Rossert J. Drug-induced acute interstitial nephritis. *Kidney Int* 2001; 60:804.
2. Rossert JA, Fischer EA. Acute interstitial nephritis. In: *Comprehensive Clinical Nephrology*, 2, Johnson RJ, Feehally J. (Eds), Elsevier Limited, Philadelphia 2003. Vol 1, p.769.
3. Neilson EG. Pathogenesis and therapy of interstitial nephritis. *Kidney Int* 1989; 35:1257.
4. Kodner CM, Kudrimoti A. Diagnosis and management of acute interstitial nephritis. *Am Fam Physician* 2003; 67:2527.
5. Wang YC, Lin YF, Chao TK, et al. Acute interstitial nephritis with prominent eosinophil infiltration. *Clin Nephrol* 2009; 71:187.
6. Ten RM, Torres VE, Milliner DS, et al. Acute interstitial nephritis: immunologic and clinical aspects. *Mayo Clin Proc* 1988; 63:921.
7. Michel DM, Kelly CJ. Acute interstitial nephritis. *J Am Soc Nephrol* 1998; 9:506.
8. Praga M, González E. Acute interstitial nephritis. *Kidney Int* 2010; 77:956.