Familial Inheritance of Rifampicin Hypersensitivity Presenting as Acute Renal Failure

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Abstract

Rifampicin is an essential component of the currently recommended regimen for treating tuberculosis. Rifampicin induces rise of hepatic enzymes and renal toxicity. Phenotype individual may be slow acetylators leading to poor urinary excretion. The exact genesis of the case report should unravel more details genetically like HLA typing.

Introduction

Rifampicin is an essential component of the currently recommended regimen for treating tuberculosis. Serum half life of rifampicin and the proportion of the unchanged drug excreted in the urine increases steadily as the individual dose is increased from 300 mg to 900 mg; probably as a result of biliary excretion route becoming saturated. Due to rifampicin there is induction of hepatic enzymes which deacetylate the drug reducing significantly half life of unchanged drug also through urinary excretion.1

Case Report

Two case reports of rifampicin inducing renal failure are as follows :-

Case 1

Ms SVS Age 14 years, complaint of fever since 1 month, weight loss and anorexia.
O/E Thin build cervical lymph nodes (anterior) palpable discrete and movable. BP 110/70 mm Hg in supine position. Pulse 100/min, Resp rate 22/min RS :- Diminished air entry on right side CVS :- NAD
GIT :- NAD.

Investigation

X-ray chest : Pleural effusion Rt. side
Pleural fluid : Yellow, Cobweb present protein 3.4 gm% Glucose 35 mg/dl Total WBC count 4300 cells/ cumm D/C Neutrophils 06% Lymphocyte 94% No organisms seen in Gram staining No AFB detected on ZNCF staining. Pleural fluid Adenosine deaminase was raised 80 U/L (Less than 40 U/L – Negative in between 40-60 U/L. Suspected more than 60 U/L- Positive) Routine haematology normal LFT Normal. Creatinine 0.8 mg% BUN 10 mg%

Family History

Father : TB Meningitis treated without any side effects. Mother : Pulmonary Koch’s treated but had developed ARF Brothers : Two, Sister : One – No major illness.

Diagnosis : Tuberculous pleural effusion

Treatment : Patient was treated with AKT 4 regimen.

Case 2

Mrs. S, age 30 years, complains of extreme weakness with fever since 6 months. O/E thin build BMI 18, CVS, RS, GIT Normal. BP 90/70 mm Hg in supine position, Pulse 94/min RR 20/min F/H father treated for pulmonary Koch's without side effects. Mother treated for abdominal Koch's had history of drug hypersensitive reaction.

Investigation CBC – Haemoglobin 8.0 gms%, WBC count 6,800/cumm, RBC count 2.8 mil/cumm, D/C N 40%, L 60%, ESR 80 mm at the end of one hour, Hypochromic normocytic anaemia. X-ray chest bilateral infiltration of apical zone HIV : Seropositive CD4 350/cmm CD8 890/cmm LFT normal diagnosis seropositive pulmonary Koch’s
Treatment - patient was treated with AKT4 regimen.

Discussion

Both cases developed drug hypersensitive reaction within a week’s time. Drugs were withdrawn after which they improved with respect to the adverse symptoms like acute shut down of kidney function and albuminuria, nausea, vomiting, flu syndrome.

Adverse reaction was brought to medical attention, patient was admitted and investigated. In both the cases haematological parameters were normal. Renal functions were abnormal showing rise in creatinine levels to 2.8 mg% and 3.2 mg%. Electrolytes K+ was 5.8 mEq/L Liver function tests were slightly altered viz SGPT 45 U/L SGOT 52 U/L ECG : WNL USG Abdomen : Normal O/E Palpation revealed pain in renal angle; Kidneys were not palpable; BP 110/70 mm Hg in supine position; Pulse 80/min.

The flu syndrome, abdominal discomfort and renal function improved spontaneously after stopping antituberculosis drugs. As rifampicin was given acute renal failure was suspected, both patients were restarted with isoniazid, ethambutol, pyrazinamide and ofloxacin.2-4

Both the cases tolerated the treatment uneventfully and thus sustained the impression that the severe drug reaction was due to rifampicin.5 In both the cases there was a strong F/H of tuberculosis; father tolerated the treatment very well but mother in both the cases had H/O severe intolerance to antitubercular drugs. The probable reasons could be slow acetylators, poor urinary excretion of unchanged drugs.2-4

There is considerable confusion in the literature regarding the acetylator phenotype and hepatotoxicity.3 Gurumurthy et al in a study of 3000 patients demonstrated that there was no relationship between acetylator phenotype and the incidence of hepatotoxicity, but phenotype individual may be slow acetylator leading to poor urinary excretion of unchanged drug causing renal toxicity, also there may be rifampicin induced immune complex formation causing change of permeability of GBM.6 Both these patients may have inherited a predisposition from their mother. Further exact genesis in both these cases should rule out or unreveal for more details genetically like HLA typing, etc.

References