Acute Liver Failure Secondary to Paracetamol Toxicity in a Malnourished Patient

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INTRODUCTION

Paracetamol has been most widely used as an antipyretic and analgesia medication worldwide as it is readily available at over-the-counter pharmacies and stores. The drug is considered safe at the usual therapeutic dose (4000 mg in 24 hours). Paracetamol overdose is known to cause drug-induced liver injury and acute liver injury(ALI) and has been recognized since 1966 to cause fatal and nonfatal hepatic necrosis. There were few cases of ALI with therapeutic doses in susceptible individuals (for example, co-existing liver disease). We present a case of acute liver failure in a nontoxic dose of paracetamol in a malnourished cancer patient.

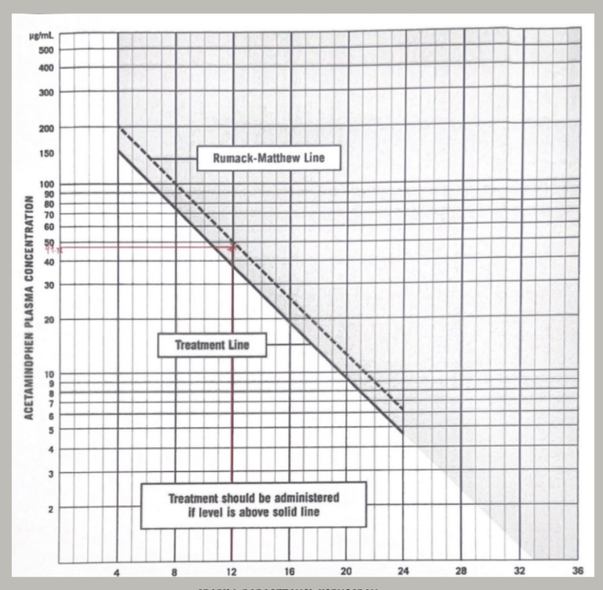
CASE PRESENTATION

A 46-year-old lady with left tonsil squamous cell carcinoma(SCC), post bilateral tonsillectomy completed radiotherapy and hypertension, was admitted for septic shock secondary to right parotitis. She received Intravenous (IV) Augmentin 1.2g TDS and IV paracetamol 1g 6 hourly. Three days after treatment in the ward, she was referred to intensive care (ICU) for ALI with reduced consciousness and required intubation. The initial investigation showed acute liver failure features with serum ammonia of 211.7 micromol/L. AST level was 8485U/L, ALT level was 5508U/L, and ALP was 282U/L. Initial investigations to rule out causes showed that viral screening was negative. An abdominal ultrasonogram showed acute cholecystitis with no evidence of biliary dilatation. The paracetamol level was 49.764mcg/ml, and The paracetamol level was 49.764mcg/ml. She was diagnosed with acute liver failure secondary to paracetamol toxicity, with King's College criteria for paracetamol toxicity was 2. The RUCAM score was 6. The patient received IV N-acetyl cysteine per protocol with a dose of 7 grams over 16 hours. Subsequently, liver enzymes showed a decreasing trend, as illustrated in Table 1, and she recovered from ALI with the treatment of N-acetyl cysteine. The patient was treated for 12 days in intensive care due to hospital-acquired infection and discharged to the surgical ward for continuation of care.

DISCUSSION

Cancer is known to be an independent factor for malnutrition. Malnourished patients are susceptible to paracetamol toxicity with regular dosing of paracetamol. This is attributed to glutathione deficiency, required for inactivation of N-acetyl-p-benzoquinonimine(NAPQI), the toxic metabolite of paracetamol.

Studies have demonstrated that doses as low as 0.5-3g of paracetamol begin to deplete glutathione levels. Mechanisms implicated include impaired degradation and secretion of lipids, resulting in the depletion of amino acids and starvation-induced autophagy, thus causing impaired paracetamol metabolism. In addition, human and animal studies have demonstrated reduced paracetamol clearance in malnourished states.



GRAPH 1: PARACETAMOL NORMOGRAM

CONCLUSION

Based on our limited experience, we propose a proper evaluation of medications dosing, especially in susceptible groups. The dose of hepatotoxic drugs should be reduced from the standard dose with proper monitoring of liver function to avoid acute liver injury.

LFT	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
ALT	5508	3809	2543	1876	548	311	603
AST	8085	5896	3471	1413	1584	795	203
ALP	127	105	148	165	160	165	189
Albumin	20	23	27	23	23	27	26
Total bilirubin	66	54	108	133	150	174	180

TABLE 1: LIVER FUNCTION TEST TREND

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