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Cholestasis induced by carbimazole; a case report: Dr K Vithian, Specialist Registrar, Colchester General Hospital

Mrs L W a 85 year old lady with past history of dementia, osteoporosis, congestive cardiac failure and recurrent shoulder dislocations was admitted from a residential home with increasing confusion. She was on strontium ranelate, adcal, aspirin, furosemide and simvastatin.

She was found to be in fast atrial fibrillation and had some signs of pulmonary congestion. Her admission blood tests were normal apart from a raised urea. Her liver function tests on admission were normal (AST 26 ALP 99). Thyroid function tests showed that she was thyrotoxic with fT4 42 and TSH<0.03. Her TPO antibodies were negative. She was started on carbimazole 20mg od. Due to multiple social problems she remained on the ward for a considerable length of time.

Repeat liver function tests showed that her GGT and alkaline phosphatase were increasing (AST 50, GGT 748, ALP 440 and bilirubin 74). Liver ultrasound, hepatitis serology and auto-immune markers were all negative. There was no significant change in her medication apart from the initiation of carbimazole and we postulated that the cholestasis was due to carbimazole. Carbimazole was discontinued and this resulted in improvement of her cholestasis. In view of her persistent thyrotoxicosis, we cautiously started her on propylthiouracil. Fortunately this did not affect her liver and her liver function tests normalised (AST 10, ALP 137) as well as her fT4 levels (17.6mmol/l).

Discussion
Thyrotoxicosis itself is associated with some degree of abnormal liver function tests in 75% with raised bilirubin (30%), raised alkaline phosphatase(60%) and raised transaminases (26%) 
However in our patient the results were grossly abnormal and the derangement was triggered by carbimazole therapy. Thionamide associated hepatotoxicity is uncommon (0.1-0.2%).

Carbimazole and propylthiouracil are associated with distinct forms of hepatotoxicity. Whereas carbimazole causes predominantly cholestasis, propylthiouracil is associated with hepatocellular necrosis. Carbimazole causes intracanalicular cholestasis and mild perportal inflammation. Slow recovery on discontinuation is usually the rule. In contrast propylthiouracil induces an allergic mediated hepatitis causing marked elevations of transaminases and submassive or massive necrosis on liver biopsy. The liver damage does not always improve despite drug discontinuation and case fatality reports of up to 25% have been reported. Occasionally liver transplantation is required.

As both drugs induce liver damage in different mechanisms it is possible to substitute thionamides with little risk of inducing further liver injury. This is exemplified in our case report where there was an excellent result with propylthiouracil with normalisation of liver function tests.

References
1. Diagnosis and treatment of Graves disease, De Groot, thyroid manager.org; 02/02/07 Chapter 11
3. Fifty years of experience with Propylthiouracil associated hepato-toxicity: What have we learned? Katherine Williams et al, JCEM 1997;82:(6):1727-1733