Letters to the Editor

Carbamazole-resistant thyrotoxicosis

Sir,

We read with interest the report of two cases of thyrotoxicosis apparently resistant to high doses of carbamazole.1 In searching for the cause of a poor therapeutic response to antithyroid drugs, several possibilities must be considered. As pointed out by Cooper,1 no definite hypothesis can be advanced to explain the most probable cause of treatment failure. In his study, among nine patients referred for nonresponse to high doses of propylthiouracil, only one was finally considered hormone resistant. However, even if it is unusual, Li et al recently reported a case of true resistance to methimazole confirmed by the determination of serum and intrathyroidal methimazole concentration.2

In our own case, reported by a Japanese group, thyroid levels were not measured. However, the hypothesis of resistance to carbamazole could have been tested alternatively by performing a perchlorate discharge test four hours after taking the antithyroid medication.3 A negative perchlorate test indicating an inadequate blockade of iodide organification and thus a possible carbimazole resistance, a positive test indicating the possibility of some degree of iodide organification block, and, therefore, a possible lack of compliance.2

Regardless of the problem of compliance, iodine contamination should be ruled out by measuring urinary iodine excretion. Iodine does affect the response of the thyroid to antithyroid drugs, directly altering the intrathyroidal metabolism of the drug and indirectly by increasing the thyroid stores of prodrug, delaying the response to treatment.4 Such mechanisms are involved in the resistance to antithyroid drugs of amiodarone- or iodine-induced thyrotoxicosis which may persist for months. One explanation for carbimazole-contaminated drug partially or totally resistant to antithyroid drugs may show a dramatic response to glucocorticoids,5 as the two cases reported here show. Therefore, we think that an unsuspected iodine contamination may have played a role in the unresponsiveness of these two patients to high doses of carbamazole and should have been discussed.

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Gastrointestinal disorders in Parkinson’s disease

Sir,

Gastrointestinal disorders are common in Parkinson’s disease. Although the underlying pathophysiology remains largely unknown, enteric nervous dysfunction and subsequent neuronal and enteric bacterial overgrowth may be important factors contributing to small bowel bacterial overgrowth with malabsorption and then enteric dysfunction. Davies et al6 recently reported the use of lactulose hydrogen breath test to study whether increased oro-cesophageal transit time and small bowel bacterial overgrowth could explain weight loss in Parkinson’s disease. None of their 15 patients showed an elevated breath hydrogen, which led the authors to conclude that bacterial overgrowth is not a major cause of weight loss. We object to this conclusion for several reasons. First, the lactulose hydrogen breath test is a questionable tool to diagnose small bowel bacterial overgrowth.7 The conditio sine qua non for this test is the presence of a hydrogen-producing flora, but in 15–20% of tested subjects the gut flora will not meet this condition.3 Therefore, the fact that none of the patients studied by Davies et al6 had an early rise of breath hydrogen excretion does not exclude small bowel bacterial overgrowth. Furthermore, the authors cite the study by Metz et al6 as evidence that the lactulose hydrogen breath test has a rather poor sensitivity (approximately 67%).8 Preferentially, the authors should have followed the recommendation of Metz et al6 to use a combination of breath tests to screen for small bowel bacterial overgrowth. Alternatively, the authors could have used the more invasive method of quantitative radiolabelled duodenal or jejunal aspirates, which remains the most accurate diagnostic tool to demonstrate small bowel bacterial overgrowth, especially when gastrointestinal motility disorders are suspected.9

Second, one would have expected to find small bowel bacterial overgrowth since oro-cesophageal transit time was increased in 10 of the 15 patients with Parkinson’s disease. Disordered small bowel motility is an important risk factor for small bowel bacterial overgrowth.6 Historically, observations suggest that impaired gastrointestinal motility might be related to impairment of the gastrointestinal myenteric plexus, which appears to be affected in Parkinson’s disease.7 Third, Davies et al6 found high lactulose/mannitol ratios in their patients, suggesting a reduction in the absorptive surface area of the small intestine. This might indicate the existence of small bowel bacterial overgrowth, since it is a well-known cause of intestinal mucosal loss, operation of brush border enzyme activity and resultant malabsorption.8 Moreover, they give no histological data to prove the absence of intestinal bacterial overgrowth.6 In conclusion, the study of Davies et al6 does not exclude the possibility that small bowel bacterial overgrowth, due to disturbed small bowel motility, may at least partially explain weight loss, malabsorption and other gastrointestinal disorders in Parkinson’s disease.

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Oxidative haemolysis after spironolactone

Sir,

I report a case of spironolactone-induced acute haemolysis in a glucose-6-phosphate dehydrogenase (G6PD)-deficient patient confirmed by rechallenge.

A 48-year-old woman was hospitalised with complaints of malaise, weakness, abdominal and lumbar pain 24 h after initiation of treatment with oral spironolactone (1 g bid) for fever and symptoms of an upper respiratory tract infection. Eight years prior, she was diagnosed with G6PD-deficiency, and A-deficiency was diagnosed, when she suffered from several sulphonamide- and acetanilide-induced haemolytic episodes requiring blood transfusions. The laboratory data were: haemoglobin 7.7 g/dl, haematocrit 22.4%, reticulocyte count 4.5%, whole blood count 12.4 x 10^6/l, platelet count 224 x 10^9/l. The lactate dehydrogenase concentration was markedly elevated (1823 U/l, normal < 300). Three days after the spironolactone therapy, she was afebrile but nauseated, icteric, and passing dark urine. The level was 3 cm below the right costal margin and the spleen was not palpable. Serum bilirubin was 2.9 mg/dl (normal < 1.0 mg/dl) with preponderant unconjugated bilirubin fraction (2.8 mg/}


3 Li H, Oshawa J, Akazuki T, Mori T. A hyperthyroid patient with Graves’ disease who was strongly resistant to methimazole: investigation on possible mechanisms of resistance. Endocrinology 1995; 42: 677–704.
