THYROID FUNCTION

Sorafenib alters metabolism of T_3

Small molecule inhibitors of tyrosine kinase activity, such as the anticancer drug sorafenib, could influence the metabolism of circulating thyroid hormones. "Sorafenib therapy led to increased iodothyronine deiodinase activity, as proven by a decreased ratio of free T_3 to reverse T_3. This finding indicates that sorafenib induces type 3 deiodinase activity and thereby leads to decreased serum T_3 levels," explains corresponding author Johannes Smit (Leiden University Medical Center, The Netherlands).

Treatment of cancer patients with broad spectrum tyrosine kinase inhibitors can alter thyroid function. Smit's team hypothesized that increased metabolism of thyroid hormones by iodothyronine deiodinases could contribute to the observed effects of these drugs. They decided to test their model in a group of athyreotic individuals.

The researchers enrolled 32 patients with progressive or metastatic medullary thyroid carcinoma in a 26-week, open-label, single arm, phase II trial of sorafenib. All participants required levothyroxine; the daily dose was adjusted to maintain TSH levels <0.1 mU/l. Thyroid function was assessed at baseline and at study end.

Smit's team found that serum free T_3 and T_4 levels were decreased, and serum TSH levels increased, after treatment with sorafenib. In addition, the ratios of free T_3 to free T_4 and free T_3 to reverse T_3 decreased, compatible with increased activity of the type 3 deiodinase. Potential effects of sorafenib on thyroid hormone binding proteins were ruled out.

The findings of this study could have implications for clinical practice. "Doctors should be aware of this phenomenon and adjust levothyroxine dosages guided by serum TSH levels," Smit concludes.

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Original article Abdulrahman, R. M. *et al.* Sorafenib-induced hypothyroidism is associated with increased type 3 deiodination. *J. Clin. Endocrinol. Metab.* doi:10.1210/jc.2009-2507