Thyroid autonomy

A difference is made between toxic multinodular goiter (disseminated thyroid autonomy) and localized autonomous thyroid autonomy, see autonomous thyroid adenoma. According to the current state of knowledge, thyroid autonomy includes diseases with varying pathogenetic mechanisms.

Toxic multinodular goiter (disseminated thyroid autonomy) is a more frequent cause of hyperthyroidism than Graves' disease in areas with iodine deficiency, e.g. in southern Germany. The reasons for this statistically close clinical correlation have not yet been fully clarified. In countries with sufficient/high iodine supply (e.g. USA), disseminated autonomy (toxic multinodular goiter) is a rather rare disease, also see pathogenesis of thyroid autonomy.

Recent findings, especially those of H. Studer's study group, have definitively marked our picture of the pathogenesis of disseminated thyroid autonomy: In the thyroid of every person, there are cell clones with varying degrees of function and different growth capacity. Some cells are capable of autonomous function and growth from the start. The term "autonomous" may mean that both function and growth are involved or that function alone is autonomous in some cell clones. There are even thyroid areas, which are scintigraphically "cold" but continue to grow under levothyroxine therapy. In a thyroid follicle, individual cells may possess very different abilities for cell proliferation and function.

In the clinical course, a diffuse "euthyroid" goiter (endemic goiter, sporadic goiter) initially develops with normal echo texture in the ultrasound and normal values for serum TSH, fT4 and fT3. Levothyroxine or iodine therapy (iodine not in sporadic goiter) at this stage usually leads to extensive regression of the goiter (also see endemic goiter). If therapy is not performed in this initial stage - including a consequent, adequate iodine prophylaxis after goiter regression (not in sporadic goiter) - disseminated autonomy may develop through a proliferation of autonomous cell clones. One of the first laboratory signs is a reduction of the serum TSH value in the gray area between euthyroidism and hyperthyroidism (i.e. at the lower limit of the normal range), and finally the serum TSH
value is no longer detectable with second and third generation methods. The prevalence of thyroid autonomy in iodine-deficient regions indicates that a particularly high iodine deficiency is an important triggering factor: A hypothesis favors a favorable proliferative effect of certain cytokines that is increased by iodine deficiency (iodine is by itself a thyroid regulatory agent, both on the functional and the growth sides). TSH seems to play a rather subordinate role here (see simple goiter). This continuous stimulation may then lead after several years to the transformation of predestinated cells into autonomous cells (Studer et al. Endocr Rev 1989; 10: 125 and Endocr Rev 1995; 16: 411; Derwahl et al. J Clin Endocrinol Metab 1999; 84: 829).

Data from two study groups indicate that activating mutations of TSH receptors are responsible for the last developmental stage of toxic multinodular goiter (Gabriel et al., J Clin Endocrinol Metab 1999; 84(9): 3328; Holzapfel et al. J Clin Endocrinol Metab 1997; 82(12): 4229).

The thyroid hormone values may remain in the normal range for several years. Toxic multinodular goiter ultimately develops. Some patients become hyperthyroid, especially after iodine exposure.

In rare cases, autonomous goiter may also develop from longstanding sporadic goiter. However, the pathomechanism has not yet been clearly defined.

Also see:
- Autonomous thyroid adenoma
- Hyperthyroidism
- Pathogenesis of hyperthyroidism
- Iodine - induced hyperthyroidism
- Nodular goiter
- Endemic goiter
- Sporadic goiter.