MULTIPLE ENDOCRINE NEOPLASIA (MEN) - LIKE SYNDROME AND OTHER HORMONAL FACTORS OF PROMOTION AND PROGRESSION OF THYROID GLAND CANCER IN MALES-LIQUIDATORS OF CHERNOBYL ACCIDENT CONSEQUENCES

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ABSTRACT

The clinical and laboratory endocrinological screening performed in 1,000 males - liquidators of Cernobyl accident consequences revealed hormonal factors leading to node formation and having unfavourable influence on progression and promotion of thyroid gland cancer.

The factors include syndrome of low thriiodothyronine, hyperprolactinemia, latent hypothyrosis and increased production of thyroglobulin.

Peculiarities of hormonal status in liquidators allow us to suggest the presence of MEN-like syndrome among the liquidators population. Possible mechanisms of expression of RET oncogene in adults that may result in MEN- like syndrome have been discussed.

The experiments on animals demonstrated multistage character of thyroid carcinogenesis.

The recent studies made in 1,000 males-liquidators in 5-10 years after the accident show the most important factors contributing to promotion and progression of radiation-induced damage of thyroid gland to be the following:

- hyperprolactinemia
- the syndrome of low level of triiodothyronine (low T_3)
- latent hypothyrosis
- increase in thyroglobulin level

The interaction of these factors leading to the formation of both small (diameter less than 1 cm) and large (diameter more than 1 cm) sonographic nodes in thyroid gland which represent the stages of thyroid carcinogenesis, is shown in fig.1.

Prolactin is known to be tumor promotor and mitogen in mammalian [1]. It has been shown that hyperprolactenemia serves as a marker of the progression and severe course in a number of tumor disorders such as breast carcinoma, cervical carcinoma, colorectal carcinoma, leukemia.

The decrease in the triiodothyronine (T_3) level is characteristic of some severe nonthyroid general somatic diseases and some nonthyroid cancers.

At present the study of oncogene RET is considered to be essential in pathogenesis of thyroid gland cancer [2,3].

This oncogene is expressed in both papillary as well as radiation-induced thyroid gland cancers, and medullary cancers arising from C-cells which generally have genetic origin.

MEN syndrome is characterized by the presence of hyperplasia or carcinoma of two or more endocrine glands [4].

The evidence of medullary cancer of thyroid gland is one of the masnifestations of multiple endocrine neoplasia (MEN) syndrome of the 2nd type.

The study by V.A. Mishagin [5] demonstrated that exposure of thyroid gland in the dose range 200-500cSv as a result of Cernobyl accident resulted in the stimulation of thyroid gland C cells.

The characteristic feature of MEN syndrome of the 1st type is the combination of hyperplasia of parathyroid gland, pituitary adenomas and hyperproduction of gastrointestinal tract hormones.

Our studies showed high incidence of hyperprolactinemia in males-liquidators that amounted up to 22%.

26% of liquidators had colonic polyps and elevated histamine - induced stomach secretion.

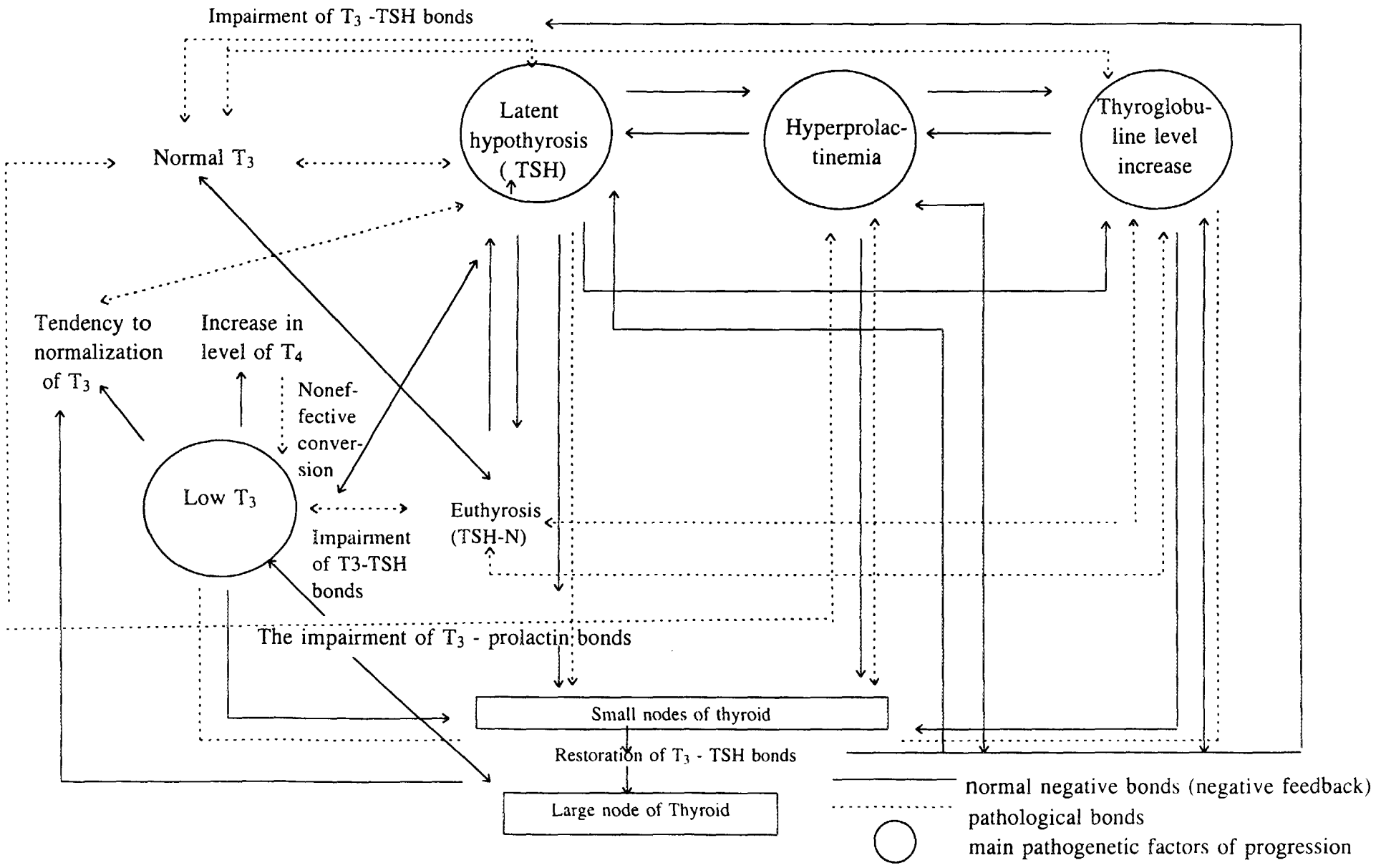

Fig. 1 Progression of nodular formation in thyroid gland in male-liquidators

The tendency to the decrease in mineralization (decrease in BMD) in bones of lower extremities and the increase in bone density in upper extremities under normal values of BMD in liquidators of 1986, found with the help of densitometry by the method of "total body", as well as the presence of osteoporosis of the whole body in some liquidators makes us to suspect the presence of hyperparathyroidism in a group of the individuals studied.

The MEN II syndrome is usually associated with medullary thyroid gland cancer and pheochromocytoma.

We followed up some liquidators with adrenal hyperplasia and the evidence of vanillylmandelic acid excretion. Thus there occurred hormonal shift in the spectrum similar to multiple endocine neoplasia syndrome.

The prognosis of the course of MEN is known to be quite favourable for life and decades may pass between the manifestations of hyperplasia of the second glands. Among 10 thousand of males liquidators of the North-Westen region of Russia followed up for eight years six histologically verified cases of thyroid gland cancer have been reported, with follicular cancers being predominant.

The presence of unstable genome in males liquidators of the Gernobyl accident consequences has been proved.

MEN like syndrome observed in liquidators is likely to be the reflection of genome instability at hormonal level.

Thus one can make a conclusion that RET oncogene expression in infancy leads to the development of papillary cancers, whereas in adults C-cells of the thyroid gland are activated and MEN like syndrome develops.

7 of 500 males liquidators studied were supposed to have the syndrome of multiple endocrine neoplasia, but no hyperplasia or cancer of the second endocrine organ has been found.

It must be pointed out that in the process of oncogene expression RET chromosome reorganization involves the 10^{th} chromosome 10 (q 11.2 q 21) [6] and structural abnormalities in the neighbouring 11^{th} cromosome lead to MEN I development [7].

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