MUSCULAR MANIFESTATIONS IN PRIMARY HYPOTHYROIDISM

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Abstract: *A prospective clinical trial over a period of 5 years conducted on a lot of patients with primary hypothyroidism which had as purpose to determine the present muscular manifestations in this type of thyroid pathology, and also the way in which these are influenced by thyroid hormone replacement therapy.*

INTRODUCTION

Primary hypothyroidism through thyroid affection occurs in 95% of the cases with hypothyroidism due to:

1. Autoimmune mechanism, with the presence of some immune factors in the serum, most often immunoglobulins, but also humoral factors which determine the decrease of the function of the thyroid cells, by blocking the adenohypophysis thyrotropin hormone (TSH) receptors and by leading to thyroid cell lysis. Often it is considered to be an idiopathic hypothyroidism.
2. Through dysembriogenetic causes and through hormone genesis disorders: thyroid agenesis, thyroid dyshormonogenesis, enzymatic deficits, iodine transport disorders, iodine utilization disorders, iodine deficit, through goiter forming substances.
3. Post thyroidectomy – after surgery for thyroid cancer after radioactive iodine or after irradiation against larynx tumors, lymphomas, etc.

PURPOSE

We conducted a prospective clinical study supported by laboratory examinations which had as purpose to determine the muscular manifestations in primary hypothyroidism, referring to the frequency, clinical and therapeutic response of muscular determinations in this type of thyroid pathology, and revealing the diagnosis difficulties of the damage done to muscular system.

MATERIALS AND METHODS

The type of study:

The research followed the recommended methodology for conducting the prospective clinical and epidemiological studies. The study was conducted with the consent of the patients and of the Ethic Committee of the hospital and had the patients approval.

1. Choosing the subjects:

The study focused on a group of 144 patients with primary hypothyroidism, who were examined in the neurology and endocrinology sections in Galaţi Emergency Hospital, followed for a period of five years. Patients were examined clinically and paraclinically every 3 months.

Clinical examination was associated with paraclinical tests. Paraclinical data were recorded in the observations sheets.

2. Data gathering:

For the clinical diagnosis of hyperthyroidism the Newcastle index was used, and in the clinical assessment of the hypothyroidism the Billewicz index was used. For the paraclinical endocrinological diagnosis there were used: hormone dosage T3, FT3, T4, FT4, TSH, thyroid ultrasound exam and thyroid scintigraphy with 99mTcO4, in doses of 2mCi, biochemical usual tests of blood and urine.

For the study of neurological damage there were used: electroneuromyography data, motor conducting velocity (VCM), sensory conducting velocity (VCS), muscular biopsy with microscopic evaluation.

3. Processing and statistical analysis of the data:

Processing and statistical data analysis were performed using specialized software SPSS version 11. We calculated central tendency indicators (mean and standard deviation), structural indicators and frequency indicators (prevalence).

RESULTS

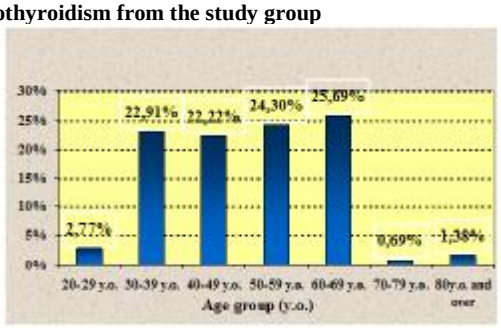
In the study group there were 144 patients with primary hypothyroidism.

Out of these, 142 were women – 98.62% and 2 – men – 1.38%.

The distribution by area of residence, urban/rural was the following: 124 patients from urban areas – 86.12%, 20 patients from rural areas – 13.88%

Age distribution of the patients with primary hypothyroidism from the study group is described in figure no. 1:

Figure no. 1. Age distribution of the patients with primary hypothyroidism from the study group



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During the follow up of the patients we have registered one death.

Out of the 144 patients, 4 were smokers.

One case was previously diagnosed with thyroid agenesis and was under thyroid hormone replacement treatment.

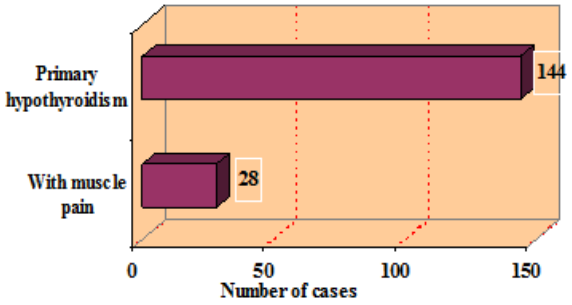
From the study group, 22 patients presented low values of T3 with T4 within normal limits. Associations of primary hypothyroidism with other diseases from the patients in the study group included: hypocalcemic tetany – 20 cases; primary idiopathic virilism – 2 cases; ovarian failure – 6 cases; obesity – 24 cases; primary hypertension – 54 cases; hypertensive cardiopathy – 6 cases; ischemic cardiopathy – 30 cases; mixedematous cardiopathy – 10 cases; chronic atrial fibrillation – 4 cases; paroxysmal atrial fibrillation – 4 cases; other rhythm disorders – 12 cases; cardiac arrest – 10 cases; conducting disorders – sinus bradycardia – 44 cases; dyslipidemia – 26 cases; decrease of glucose tolerance – 2 cases; diabetes – 2 cases; type 2 diabetes under treatment with antidiabetics administrated orally – 14 cases; urolithiasis – 14 cases; chronic renal failure – 2 cases; gall bladder stones – 10 cases; tumors – 33 cases: uterine fibroids – 20 cases; ovarian cyst – 4 cases; breast cancer – 4 cases; colon cancer – 2 cases; mediastinal lymph node tumor – 1 case; fibrocystic mastosis – 2 cases; pulmonary tuberculosis – 6 cases; hypochromic anemia – 2 cases; macrocytic anemia – 2 cases; varicose legs with pulmonary embolism – 1 case; obliterating arterial pathology of the lower limbs – 2 cases; phlebothrombosis in the lower limbs – 1 case; chronic hepatitis – 2 cases; hypermenorrhea – 8 cases; hypoanabolic syndrome – 2 cases; central adrenal failure – 2 cases; psoriasis – 2 cases; myxedematous pericardial fluid – 2 cases.

We remark an association between primary hypothyroidism with a high number of cases of tumors with various sites as well as type II diabetes, data which is consistent with that from other studies.

The encountered muscular manifestations in the study group:

Muscle pain was found in 28 cases – 19.44% of the patients with primary hypothyroidism (figure no. 2).

Figure no. 2. The frequency of the cases with muscle pain out of all the patients with primary hypothyroidism



- Subjectively the symptoms that predominated were:
  - Muscle stiffness – 8 cases (5.55%);
  - Myalgia – 15 cases (10.41%);
  - Muscle cramps – 20 cases (13.88%).
  - Slow muscle contraction and relaxation – 5 cases (3.47%);
  - Muscle fatigue, worsening overnight – 22 cases (15.27%);
  - Sensitivity during palpation of the muscle groups – 10 cases (6.94%);
  - Painful muscle spasms – 3 cases (2.08%).
- Objectively rhizomelic hypothyroid myopathy – was encountered in 3 cases from the study group – 2.77% out of all the patients with primary hypothyroidism, exclusively in women with emphasized thyroid hypofunction which was evolving, on average, for about 4 years.

The symptoms included muscle cramps and muscle weakness, decrease of muscle strength, predominantly in the belts, where there existed a mild muscle atrophy, muscle mass with increased consistency, sensitive to palpation and mild hypertrophy in the cheek muscles. The described symptoms presented a worsening over night.

Creatine phosphokinase (CPK) dosages were characteristic, registering values that exceeded 10 times the normal values.

Electromyographic examination in the tailor muscle registered a repetitive activity of pseudo myotonic type with VCS and VCM normal.

Muscle biopsy with myogenic type lesions was nonspecific.

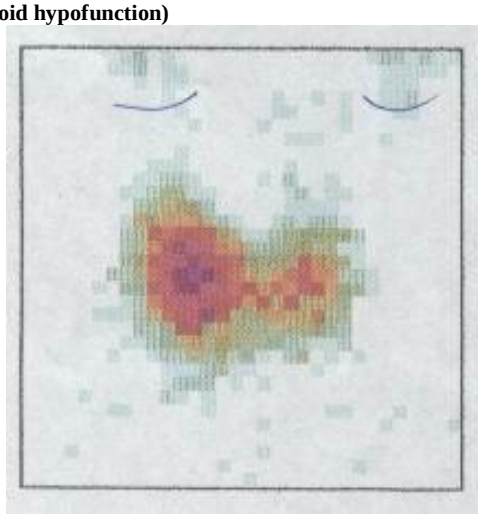
We exemplify the following case:

Patient S.C., 51 years old-admission grounds: muscle strength deficit in the belts, myalgia, muscle cramps, difficulty in walking long distances or climbing stairs. Personal history: primary hypothyroidism. Medical history: patient with primary hypothyroidism under intermittent thyroid hormone replacement treatment, is admitted for muscle strength deficit in the belts, that installed and grew progressively in several months.

Clinical exam: signs of hypothyroidism, muscle strength deficit in the belts, muscle mass painful on palpation, discreet hypertrophy in the cheek muscles, diminished equal ROT without objective sensitivity disorders.

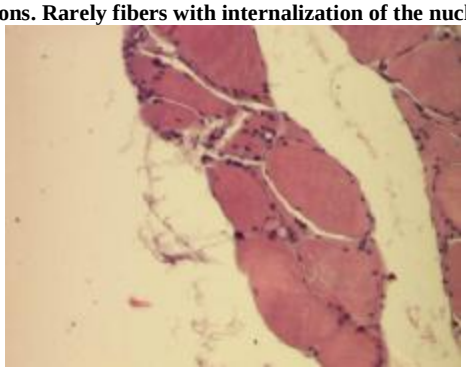
Laboratory examination: hormone dosages: T3 – 10 ng/dl, T4 – 7.21 µg/ml, TSH – 5.9 microm/ml; CPK – 480 mUI/ml; Thyroid ultrasound: right thyroid lobe of 21 mm, left thyroid lobe of 25 mm, isthmus of 10 mm with multi macronodular structure with hypoechoic areas in the center of the lobes; Thyroid scintigraphy (figure no. 3).

Figure no. 3. Thyroid scintigraphy – patient S.C., 51 years old: projection areas of the thyroid lobes are slightly reduced. Inhomogeneous capture, reduced in the left thyroid lobe. Moderate amount of free tracer in the circulation (thyroid hypofunction)



Muscle biopsy under optic microscopy revealed the following aspect (figure no. 4) of myogenic non specific suffering. H.E. staining, OB x10, O.C. x10:

Figure no. 4. Muscle biopsy – patient S.C., 51 years old: association of a group of atrophic striated muscle fibers, sometimes reduced to a "nest of nucleus" with hypertrophied muscle fibers, with the loss of muscle striations. Rarely fibers with internalization of the nucleus



VCS and VCM – normal in the external popliteal sciatic nerve;

Myopathic phenomena have improved after initiation of thyroid hormone replacement treatment, after 6 months.

DISCUSSIONS

Duyff et. al. (1) notes that muscle cramps occur in 42% of the patients with hypothyroidism, in our study – only in 13.88%.

After Uldry et.al. (2), modifications of pseudo - myotonic type occur in 55- 99% of the patients with hypothyroidism; in our study, slow muscle contraction and relaxation occur in 3.47% of cases.

Duyff (1) states that muscle fatigue occurs in 54% of the cases of hypothyroidism.

Muscle fatigue, worsening overnight occur in 15.27% of cases, in our study, result confirmed by other authors.(3,4) We have not encountered in the study group any cases of Kocher-Debre-Semalaigne syndrome (5,6) (cretinism due to hypothyroidism, associated with muscle manifestations).

As in the case of neuropathies, the data referring to the frequency of muscle sufferings in hypothyroidism are varied.(7,8) According to Uldry et. al. (2), myopathy occurs in 30-80% of the cases of hypothyroidism.

In the hypothyroid myopaty, the muscle biopsy shows type II atrophic fibers with the increasing number of central nucleus (9), fact that was confirmed even in our study.

Other studies (10) mention that myopathy is extremely rare in hypothyroidism (exceptional) or describe the hypothyroid myopathy as being proximal, associated with myalgia, muscle cramps and myoedema and having slow osteotendinous reflexes, with CPK having elevated values.

Serratrice et. al. (3) signals in hypothyroid myopathy symptoms such as hypertrophy of the cheek muscles, forearms and arms associated with spontaneous myoedema, typically associated with myotonic type phenomena. He notes even rare, proximal, atrophic forms stating that thyroid myopathy regresses under treatment

CONCLUSIONS

1. Muscle suffering of myopathic type occurs in old and neglected hypothyroidism.
2. Subjective muscle complaints of the patients with primary hypothyroidism occur in about 1/3 of the patients and consist of muscle stiffness, myalgia and muscle cramps.
3. Subjective disorders improve after thyroid hormone replacement treatment, after at least 6 months since the initiation.
4. Objective muscle affection is represented through rhisomelic myopathy, with modifications of the muscle enzymes, electrophysiological and histological characteristic signs.
5. The treatment of myopathies secondary to primary hypothyroidism includes thyroid hormones in a prolonged and sustained cure.
6. Improving the suffering caused by myopathies secondary to primary hypothyroidism occurs, on average, after 6 months since the initiation of thyroid hormone replacement treatment, a fact confirmed also by other studies.
7. The cases of myopathy encountered in our study group had a lower frequency than those quoted in other studies.

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