MUSCULOSKELETAL IMPAIRMENT IN PRIMARY HYPOTHYROIDISM

Iuliana Radu1, Liliana Groppa1*, Lorina Vudu2
State University of Medicine and Pharmacy “Nicolae Testemitanu”- Chisinau, Republic of Moldova
1. Department of Internal Medicine, Rheumatology and Nephrology
2. Chair of Endocrinology
* Corresponding author. E-mail: lgroppa@gmail.com

MUSCULOSKELETAL IMPAIRMENT IN HYPOTHYROIDISM (Abstract): This article contains bibliographical data concerning the rheumatic clinical manifestations in hypothyroidism: polyarthralgias, lack of recent skill of fine movements of the hands, carpal tunnel syndrome or tarsal, degenerative arthropathy or acute type (gout, chondrocalcinosis), adhesive capsulitis (frozen shoulder syndrome), generalized muscular stiffness, hypothyroid myopathy, secondary osteoarthritis, Dupuytren's contracture, “trigger finger” (also called as stenosing tenosynovitis or trigger thumb) etc. and data on the short history, epidemiology, of these disorders. Review include 60 bibliographical sources. Keywords: PRIMARY HYPOTHYROIDISM, MUSCULOSKELETAL IMPAIRMENT, RHEUMATIC DISEASES.

Thyroid hormones (THs) are vital role for maintaining the body’s homeostasis. Thyroid hormones are among the key regulators of metabolism, adjusting the amount of proteins, carbohydrates, fats and minerals used by the body (1). Thyroid hormones play an important role in the development, maturation and maintaining morpho-functional integrity of the musculoskeletal structures (2). At the same time the decreasing synthesis of thyroid hormones leads to multiple negative effects on the entire system of the body functioning (1). Hormonal deficiency has unfavorable effects on bone formation and modeling, with consequences on the neuromuscular function and bone density. The relationship between musculoskeletal impairment and those of thyroid contains more aspects, among which, is, certainly, the imitation of the rheumatic diseases (2).

Currently thyroid gland pathology is considered one of the most common endocrine diseases in structure (3). A major endocrine pathology, involving various organs, frequently associated with musculoskeletal impairment presents, primary hypothyroidism (hT) (4, 5, 6, 7, 8, 9).

SHORT HISTORY

The relationship between arthritis and thyroid disease is known for a long time, in particular, the appearance of association with hypothyroidism (10). It is described for the first time in 1892, as the hypothyroid myopathy with endemic cretinism in children by E. Cochër, subsequently, defined as Kocher-Debré-Séméaigne syndrome. In 1897, Johann Hoffman, for the first time, described a similar syndrome in adults, in a patient after thyroidectomy, which was later named in honor of this
The relationship between thyroid disorders and shoulder pain was noticed in the first half of the 20th century (13). In 1960 was described the arthritis association with subclinical hypothyroidism, in the same time with the introduction of radioimmunoassay examination for thyroid stimulating hormone (TSH). The description of thyroid autoantibodies in the 50-s and 60-s of the last century forms a new stage in association of autoimmune thyroid disease (AIDT) with other diseases (14).

**EPIDEMIOLOGY**

In the Republic of Moldova, the thyroid pathology is ranked at the moment, the second disease as frequency among endocrine affections, leaving the first place only for diabetes. Comparing to year 2000, by 2006 the number of patients with thyroid pathology doubled (15). According to the data of specialized literature, 2-6% of the population suffer from hypothyroidism (16). The prevalence of subclinical hypothyroidism in the general population ranges between 1,3% -17,5%, depending on age and sex of the patient. The incidence of subclinical hypothyroidism is higher in women than in men, increasing with age and reaching 21%, in women, and 16% in men, aged over 74-years-old (17). Epidemiological studies indicate that the global prevalence of manifest hypothyroidism in population is 0,2-2%, subclinical 7-10% among women and 2,3% among men. In the group of older women, the prevalence of all forms of hypothyroidism can reach 12% or more (3). The estimates of the study conducted by NHANES (National Health and Nutrition Examination Survey) III highlight the prevalence of hypothyroidism in the US population which constitutes 4,6% in general population (0,3% clinical and 4,3% subclinical). In addition, this study found that prevalence rates increase with age and may approach up to 20% in women, from the general healthy population in the postmenopausal period (18). According to the results of a similar study conducted in Norway, the prevalence of diagnosed hypothyroidism is 4,8% in women and 0,9% in men (19).

According to I. Atroshi et al. (20) the prevalence of carpal tunnel syndrome (CTS) in the general population is 3,8%. However, M. Cakir and co-workers (6), reported that 9,5% of patients with thyroid disease have CTS, this phenomenon is more common among patients with hypothyroidism (30,4%). Women are affected more frequently (21). According to other studies, carpal tunnel syndrome occurs in approximately 30% of patients with hypothyroidism (22, 23).

Arthropathy occurs in 20-25% of patients with myxedema (8). Dupuytren's contracture, limited joint mobility and CTS are more common in patients with hypothyroidism, which are- 21,7%, 8,7% and 30,4%, respectively, and the "trigger finger "(TF), occurs in 10% of patients with subclinical hypothyroidism, which correlates with positive anti-thyroid peroxidase (anti-TPO) antibodies (6). Men are affected 7 times more often than women by Dupuytren’s contracture, especially those aged over 40-years-old (24). The prevalence of fibromyalgia in AITD is determined at 30 to 40% of the patients (25, 26, 27).

**CLINICAL MANIFESTATION**

Rheumatic diseases are increasingly recognized as having an important role in de-
terminating the health state of the population, and by diverse spreads, these diseases can be ranged from simple localized pain to the onset of disability movement (28).

Rheumatic clinical manifestations, produced by hypothyroidism are: polyarthralgias, lack of recent skill of fine movements of the hands (29), CTS (rarely tarsal), degenerative arthropathy or acute type (gout, chondrocalcinosis), adhesive capsulitis (frozen shoulder syndrome), generalized muscular stiffness, hypothyroid myopathy (2, 30), secondary osteoarthritis (OA) (31), Dupuytren's contracture, TF (also called as stenosing tenosynovitis or trigger thumb) (6), and of association with autoimmune diseases (vitiligo, rheumatoid arthritis (RA), Sjögren's syndrome, systemic lupus erythematosus (SLE), chronic active hepatitis, systemic sclerosis), which can dominate the clinical picture and serve as the only manifestation or symptom of the disease (32).

According to V. Nasonova and N. Bunchyuk (33), in hypothyroidism, some patients may develop knee ligamentous weakness device, and Baker's cyst formation. Arthropathy is manifested by stiffness, joint swelling, sometimes the appearance of non-inflammatory joint effusion of articular cavity. Rheumatic manifestations can occur even in euthyroid patients, but more frequently in patients with hypothyroidism, in comparison with healthy persons without affecting the thyroid gland (34).

Carpal tunnel syndrome occurs when there is a compressing of the flexor tendons and the median nerve that travels through the carpal tunnel, patients usually present with pain, numbness or tingling in the median distribution (in the first two fingers and the side of the median third). These symptoms may worsen especially at night or at wrist flexion. In cases of prolonged physical activity, a weakness or atrophy of the thenar muscle may occur (35). Bilateral carpal tunnel syndrome has been reported in hypothyroidism by JC Jr. Chisholm (36), and an increased joint laxity, due to a hyaluronate deposits frequently found, this fact is reported by R. Ionescu (21).

Tarsal tunnel syndrome, with medio-plantar nerve damage, is rarely observed (2). In these cases the patient complains pain such as burning and tingling in the big toe, planting area. Pains are nocturnal and may radiate to the back of the calf. The pain may improve while walking (24). The mechanism leading to compression is due to the accumulation of glycosaminoglycans in the surrounding tissues (2, 37).

Dupuytren's contracture is a painless condition that occurs marked thickening of the palmar aponeurosis, flexion contractures of the ring and little fingers (24, 38).

Tenosynovitis - is the most common cause of pain and disability at the level of hand. It affects flexor tendons of the fingers II-V and the long flexor of the thumb. Tenosynovitis occurs leading to fibrosis and constriction of the first fiber annular ring which covers the metacarpophalangeal (MCP) joint, being affected sliding tendon, causing pain and locking finger in flexion, especially in the morning, crepitations could be heard in the mobility (24).

Adhesive capsulitis is a painful condition, which is characterized by pain on movements and restriction in all dimensions, in the absence of joint damage. The progression of the disease has three phases:

- Painful phase- gradual onset of diffuse shoulder pain irradiated mobilization especially in the level of trapezius muscle. Sub-
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sequently, the pain becomes nocturnal, waking the patient up from sleep for weeks - months;

• Adhesive phase (the stiffness). The pain becomes less severe, no longer appears in garaging or during the night, but still discomforting and feeling pain at the end of the movement. Limited movements of the gleno-humeral external rotation, internal rotation, and abduction becoming evident - up to one year;

• Resolution phase (thawing). The pain is less intense, the dominant symptom is limiting the movements of the shoulder.

A clinically useful indicator of the capsulitis presence is pain appeared during passive shoulder external rotation (21, 24).

Suffering pains. The simplest manifestations are the most common joint morning stiffness and eventual degenerative effusion. Accelerating speed of erythrocyte sedimentation rate for other reasons in some cases leads itself to confusion with rheumatoid arthritis (39). Rarely, the arthropathy is monoarticular or erosive, interestingly the interphalangeal joints can to mimic severe arthritis (40, 41). In some cases, calcium pyrophosphate dehydrate crystals were found in synovial fluid, but the condro-calcinosis association and its acute event (pseudogout) is not so frequent as in hyperparathyroidism and hemochromatosis (42). There are disputes over, whether or not there is random nature of the association between hT and chondro-calcinosis (39, 43, 44). However McCarty (45), a recognized researcher in chonrocalcinosis, says that the presence of calcium pyrophosphate dehydrate crystals in the joints is probably the most frequently associated with hT, and only then with hyperparathyroidism, hemochromatosis, and respectively, with hypophosphatasia. It was stated that in primary hT, in comparison with the general populations, there is indeed an increase in both the frequency of hyperuricemia and gout. In hT, it is affected kidney pool, by lowering the uric acid removal. hT was suspected as the trigger gout attacks (46). The symptomatology is alleviated through suppression of neutrophils (47). Hypothyroidism is linked to an increased incidence of fractures (48). It still remains controversial whether thyroid hormone replacement therapy also has adverse effects on bone. A review of 63 studies could not resolve the debate. Therefore, there is insufficient evidence on the effect of levothyroxine on the bone mineral density (BMD) (49).

After Bland et al. (50), in hT is usually affecting knees, MCP and proximal interphalangeal (PIP) joints, and as well as metatarsophalangeal (MTP), talocrural (TC) joints, without the presence of inflammatory synovitis. These impairments depend on TSH increase of the hyaluronic acid and the synthesis of proteoglycans in patients with hT (8, 50). Most cases of arthropathy change in hypothyroidism are found in adult, involving knees and hands, while the hip and femoral epiphysis occurs more frequently in children (7). Usually in hT, the syndrome of dolor palpation is missing. Generally, it affects symmetrically the knees, radiocarpal joint, small joints of the hands (PIP and MCP) and MTP joints. In some cases, there is a destructive arthropathy localized mainly in the PIP joints and less distal interphalangeal (DIP) joints (33).

In secondary OA, patients have "mechanical" type pain, stiffness from inactivity, limiting mobility, joint instability, crackling or grating sensation (crepitus)
highlighted by palpation or audible (31). In adults with hypothyroidism, joint pain can reveal an aseptic bone necrosis. Rubinstein and Brooks (51), described five patients with hypothyroidism, who were evaluated for a period of time ranging from 1 to 16 years-old, experiencing joint pain, which later were diagnosed with radiological and histological with aseptic bone necrosis. The bones involved were unilateral or bilateral femoral neck in three patients and two - to carpal bones (lunate bone or crescent) (51).

Pretibial myxedema is presented in the form of painless nodules of pink or bright red color, of various sizes, being placed on the pretibial surface, which can have a similar aspect to *erythema nodosum* (21).

**Muscle myopathy (hypothyroidism).** In this condition, the most often reported symptoms by patients are: pain, cramps, stiffness, slight fatigue, and muscle weakness. On physical examination can be revealed muscular hypertrophy, proximal muscle weakness, delayed deep relaxation phase of tendon (52). At the initial examination, there is an increase in muscle mass of several groups of muscles, including the trapezius, deltoid, rectus capitis, and gastrocnemius (32). Stiffness and muscle weakness in myopathy are diffuse (53, 54). Generalized myalgias, when accompanied by painful trigger points may suggest this diagnosis, but these nonspecific symptoms may also be an initial hT phase (55, 56). Muscle pain and a feeling of "numbness" of the muscles are frequently and aggravated by cold exposure (57). A rare clinical disorder of myopathy in severe hT is Hoffman syndrome, which is manifested by severe muscle stiffness, increased muscle mass (pseudohypertraphy), variable muscle weakness, is accompanied by high levels of creatine kinase (58). Among of muscle symptoms of - muscle proximal myopathy (hypothyroid myopathy) occurs in 25-79% of cases in adult patients with primary hypothyroidism (22, 35, 59). According to Alakes’s studies et al. (4), highlighted musculoskeletal manifestations in 120 patients with primary hypothyroidism constituted: bodily pain and myalgia - 83,33% of patients, muscle cramps and stiffness - 83,33%, back pain - 50%, arthralgia - 25%, adhesive capsulitis - 20,8%, limited joint mobility - 16,67%, myopathy - 8,33%, CTS - 6,6%, TF- 4,1% of Dupuytren's contracture - 3,33% and tarsal tunnel syndrome in 1,6% of patients. Associated rheumatologically manifestations were determined as follow: osteoarthritis - 66,7% of cases, mild inflammatory arthritis involving wrist joint - 50%, RA - 16,67%, SLE - 8,33%, fibromyalgia - 5%, Raynaud's phenomenon - 1,66% and the mixed connective tissue disease - at 1,66% of patients (4). A study conducted by Soy Mehmet et al. (60), in a group of 65 patients who were diagnosed with autoimmune thyroiditis, including 70% - with hypothyroidism demonstrated that the recorded rheumatic symptoms were as diverse as fibromyalgia - 34%, recurrent aphthous stomatitis - 18%, OA-12%, keratoconjunctivitis sicca and xerostomia - 10%, CTS - 10%, Raynoud’s syndrome - 6%, inflammatory arthritis - 6%, autoimmune - diseases 18%.

**CONCLUSIONS**

The relationship between hT and rheumatic diseases is significant and essential in the diagnosis and treatment of patients. The knowledge of spectrum of extra glandular clinical manifestations (including osteo-articular manifestations) is an im-
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Important step in the management of patients with hT. However, thyroid dysfunction should be considered in the differential diagnosis in different musculoskeletal manifestations but the investigations of anti-thyroid antibodies should be a component part of screening the patients with joint problems, because they can serve as early signs at the presence and prognosis of the disease.

REFERENCES

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