REVIEW ARTICLE

Rheumatological Manifestations in Hypothyroidism

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Many endocrine disorders are associated with well characterized rheumatic syndromes. Some of the earliest descriptions of classical endocrine diseases such as acromegaly and hypothyroidism were focused on bone, joint and muscle manifestations. The principle elements of connective tissue are cells and products of those cells whose growth and metabolism are influenced by hormone. Thus endocrine glands, through hormone action, directly affect the function of musculo-skeletal system.

The spectrum of musculoskeletal manifestations in hypothyroidism are varied. They include :

1. Rheumatoid arthritis like illness. (large joints, especially prominent in knee)
2. Pseudogout like illness
3. Hyperuricaemia/Gout.(Hyperuricaemia common ; Gout-rare)
4. Flexor tenosynovitis of the hand
5. Carpal tunnel syndrome
6. Polymyalgia like illness
7. Proximal myopathy - non-inflammatory with muscle hypertrophy (Hoffman's Syndrome).
8. Skeletal abnormalities in children, including slipped capital femoral epiphysis. (1)

1. Rheumatoid Arthritis like Illness

Bland and Frymoyer (2) in 1970 described rheumatic findings in 38 patients with frank hypothyroidism. Eleven had objective rheumatic findings. Joint involvement was concurrent with onset of hypothyroidism in 6 of 11, hypothyroidism preceded the arthropathy in 3 of 11, and arthropathy appeared first in 2 patients.

The most characteristic pattern of arthritis in hypothyroidism results in synovial thickening and effusions of large joints, especially the knees. The effusions are predominantly non-inflammatory. Most often they are bilateral. Hand joints may also be affected and this may lead to an initial diagnosis of rheumatoid arthritis. Wrist, metacarpophalangeal and proximal inter-phalangeal joints may be affected. Morning stiffness usually lasts less than 30 minutes and only a minority have signs of acute inflammation.

2. Pseudogout like Illness

Calcium pyrophosphate dihydrate crytals (both intra and extracellular) are demonstrated in hypothyroid patients with knee effusions, though acute pseudogout at presentation is rare. Some studies have documented subsequent acute pseudogout in patients with CPPD crystals in hypothyroid subjects (3). Synovial biopsies reveal mild inflammation and thickened synovium (3 to 5 layers of synovial lining cells). Sometimes effusions with CPPD crystals may be present in MCP joints. Synovial fluid analysis reveals.

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(a) Usually less than 1000 white cells/mm^3
(b) CPPD crystals
(c) High viscosity by string test.
(d) Increase in hyaluronic acid
(e) High total protein in 50% of cases.

Radiographs reveal chondrocalcinosis with initial chondral and subchondral erosions and presence of cyst-like structures. The association of hypothyroidism, true pseudogout and pyrophosphate arthropathy was reviewed by Alexander et al (4). Of the 105 consecutive patients with pyrophosphate arthropathy, 10.5% had hypothyroidism Job-Deslandre *et. al.*, in a study of 100 patients with hypothyroidism showed a 17% prevalence of chondrocalcinosis (5)

3. Hyperuricaemia/Gout

Erickson *et. al.* (6) evaluated 54 consecutive crystal proven patients with gout, prospectively for hypothyroidism. Fifteen percent of patients with gout compared with 4% of controls had elevated thyroid stimulating hormone, an average of 2.5 times higher in women and 6 times higher in men than in controls. Although hyperuricaemia is common in hypothyroidism, gout attacks are rare.

The occurrence of gouty arthritis in patients with hypothyroidism is unclear, although urate clearance is lower than in the same patients after treatment with thyroid hormone replacement therapy. Screening for occult hypothyroidism in patients with gout is recommended.

4. Flexor–Tenosynovitis of Hand

A characteristic feature of hand involvement in hypothyroidism is a flexor tenosynovitis. Flexor tenosynovitis and thickening of the transverse carpal ligament may result in carpal tunnel syndrome. While the arthropathy usually responds to thyroid hormone replacement within 2 weeks; flexor tenosynovitis may persist for weeks after the joint signs have resolved.

5. Carpal Tunnel Syndrome

Hypothyroidism was the reported cause of carpal tunnel syndrome in up to 7.6% of patients in various series (7,8). In review of all patients presenting with carpal tunnel syndrome over a 10 year period, 5 of 49 patients had myxoedema (9). Similarly approximately 7 percent of patients with hypothyroidism may have compression of the median nerve.

The aetiological background to carpal tunnel syndrome is multifactorial and includes :

1. Direct pressure on the nerve from an oedematous transverse carpal ligament
2. Flexor tenosynovitis
3. Infiltration of the perineurium and endoneurium
4. Neuronal metabolic dysfunction secondary to the hypothyroid state

Acroparaesthesias are also often a prominent component of hypothyroidism, suggesting a metabolic effect of thyroid deficiency on nerve function. Most studies of carpal tunnel syndrome caused by hypothyroidism stress the rapid resolution of symptoms with thyroid hormone replacement therapy.

6. Polymyalgia like Illness

The diagnosis of hypothyroidism should be considered in patients who have a polymyalgia rheumatica like picture and a normal or only slightly elevated ESR. Patients may also present with a fibromyalgia like picture. These presentations may be prominent in patients who have muscular symptoms as a component of a hypothyroid state.

7. Proximal Myopathy

Approximately 5% cases of acquired myopathy are due to hypothyroidism. Proximal muscle weakness occurs in about 1/3rd of hypothyroid patients. Muscle cramps, pains and stiffness occur commonly. Features of slow muscle contraction and relaxation occur in 25% of patients, and relaxation phase of muscle stretch

reflexes is characteristically prolonged. The serum CK level is often elevated (up to 10 times normal), even where there is minimal clinical evidence of muscle disease (10).

The most common finding on muscle biopsy is atrophy of Type-II fibres and absence of inflammatory changes. Electromyograms reveal myopathic potentials and show a smaller and shorter individual action potentials than normal, an increased proportion of polyphasic potentials and increased insertional activity. Fibrillations occur, but are less common (11).

The other variety of myopathy manifestating as weakness, muscular stiffness and an increase in muscle mass in an adult with myxoedema has been referred to as Hoffman's syndrome (12). The striking increase in muscle bulk may take 6-10 months to resolve with thyroid hormone replacement.

Myxoedema pseudomyotonia is muscle weakness associated with delayed muscle contraction as well as relaxation (delayed deep tendon reflexes). The electromyogram does not show the high frequency after discharge as seen in true myotonic disorders.

8. Skeletal Abnormalities in Children

Thyroid hormone is essential for normal growth and maturation of the skeleton. The effect on growth appears to be due to a stimulation of protein synthesis as well as to a potentiation of action of growth hormone. Before puberty, thyroid hormone is the major prerequisite for normal maturation of bone.

Deficiency of thyroid hormone beginning in early life leads to both a delay in the development of and an abnormal, stippled appearance of the epiphyseal center of ossification (Epiphysial dysgenesis). Linear growth is serially impaired; leading to dwarfism in which the limbs are disproportionally short in relation to the trunk. Bone age is always retarded to chronological age.

Clinical manifestations in children thus include, short statures, retarded bone age, epiphyseal dysgenesis and delayed dental development. The physeal growth plate is affected, resulting in premature closure and abnormal cartilage and bone, which may result in osteochondritis deformans and slipped capital femoral epiphysis (13).

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