

Review Article

Rheumatological Manifestations of Diabetes Mellitus — An Update

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Abstract

Diabetes mellitus (DM) is a chronic metabolic condition and a major public health problem. It is associated with many musculoskeletal manifestations which are usually under-recognized and poorly treated, as compared to other complications like neuropathy, nephropathy and retinopathy. These manifestations affect the joints, soft tissues and the bones leading to alterations in musculoskeletal system of the patient. This article reviews the major rheumatological problems of diabetes mellitus including their management.

Key words: Diabetes mellitus; Rheumatological manifestations

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Introduction

Diabetes mellitus (DM) is a chronic metabolic condition characterized by persistent hyperglycemia with resultant increased morbidity and mortality occurring as a result of associated microvascular and macrovascular complications.¹ Musculoskeletal manifestations are usually under recognized and poorly treated unlike other complications. The National Health Interview Survey in US in the year 2004 has shown that 58% of diabetic patients will develop functional disability.² The rheumatic manifestations are closely related to age³, retinopathy⁴ and prolonged disease duration.⁵

Musculoskeletal manifestations can be classified in following way.

I. Joint disorders

- (a) Limited joint mobility, also known as diabetic cheiroarthropathy or diabetic hand syndrome

- (b) Neurogenic arthropathy (Charcot joint)
- (c) Infective arthritis
- (d) Osteoarthritis
- (e) Gout and hyperuricemia
- (f) Calcium pyrophosphate deposition disease (CPPD)

II. Skin and periarticular disorders

- (a) Scleroderma diabeticorum
- (b) Dupuytren's contracture
- (c) Carpal tunnel syndrome
- (d) Trigger finger (flexor tenosynovitis)
- (e) Adhesive capsulitis of shoulder joint (frozen shoulder)

III. Muscle disorders

- (a) Myalgia
- (b) Myositis
- (c) Muscle infarction

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IV. Bone disorders

- (a) Diffuse idiopathic skeletal hyperostosis (DISH)
- (b) Osteopenia
- (c) Osteomyelitis
- (d) Osteolysis

Limited joint mobility (LJM)

It is known as diabetic cheiroarthropathy after the Greek word “Cheerios” for hand. It is characterized by thick, rigid, tight, waxy skin mainly on the dorsal aspect of the hands with flexion deformities resulting in painless marked restriction of the flexion and extension of joints, especially interphalangeal, metacarpophalangeal (MCP) and wrist joints. It is mainly a clinical diagnosis and the imaging findings are nonspecific.⁶

LJM can be shown clinically by two signs:

- a. Prayer sign – characterized by inability of the two palms to come completely together with the wrists maximally flexed
- b. Table top sign – characterized by inability to touch the palmar surface of the fingers to the table when the patient is asked to keep the palms flat on the table top

The ultrasound in LJM shows thickening of the flexor tendon sheaths and subcutaneous tissues⁶ while MRI shows thickening and enhancement of the flexor tendon sheaths.⁷ Biopsy specimens of involved skin show marked deposition of periarticular collagens rather than periarticular cartilage, which may be due to non-enzymatic glycosylation of collagen.⁸ LJM is most commonly seen in type 1 diabetes with a prevalence of 8–50%⁹ as compared to controls¹⁰. It is more commonly seen in patients with diabetic neuropathy as compared to those without it.¹¹ Treatment consists of nonsteroidal antiinflammatory drugs, physiotherapy and better glycemic control.

Charcot’s arthropathy

It is a progressive, painless and degenerative arthropathy associated with longstanding duration of diabetes, peripheral neuropathy¹², mechanical and vascular injury secondary to diabetic neuropathy^{13,14}. It is characterized by initial resorptive phase followed

by hypertrophic or repair phase.¹⁵ Clinically the patient may present with sudden onset erythema and unilateral edema of the ankle. Recurrent attacks result in collapse of plantar arch and development of bony prominences.¹⁴ Bilateral Charcot’s arthropathy is seen in 20% of the patients.¹³ Differential diagnoses are from osteomyelitis or septic arthritis. Osteomyelitis and septic arthritis are characterized by fever, raised white cell count and ESR. Initial warmth and erythema occur in both conditions. Diagnosis is established via imaging studies which should be carried out in the early disease. It shows osteopenia, reduction in joint space and soft tissue edema.¹⁶ It also shows ligamentous disruption, bone fragmentation, sclerosis and joint deformity. There is a center of signal enhancement within joints and the subchondral bone due to exudative osteomyelitis.^{17,18} Treatment goal is to maintain structural stability of the foot and ankle with prevention of skin ulceration and use of appropriate footwear. Surgery is indicated in patients with marked ankle and midfoot deformities with skin ulceration.¹⁹

Infective arthritis

It occurs more commonly in diabetics than nondiabetics due to immune-compromised state and usually involves shoulder joint. Shoulder arthritis is caused by E. Coli, pyoarthrititis of hip by Campylobacter organisms and septic arthritis of the small joints of hands by streptococcal organisms.²⁰

Osteoarthritis

It occurs commonly in diabetics and is characterized by destruction of periarticular cartilage, bony overgrowth with osteophyte formation. The postulated mechanism for degenerative changes could be decreased synthesis of polysaccharides required for the normal function of articular cartilage.²¹

Gout and hyperuricemia

Gout is a heterogenous disorder characterized by hyperuricemia and arthritis induced by accumulation of white crystals. Uncontrolled diabetes, especially DKA is a risk factor for acute gouty arthritis. Associated obesity precipitates hyperglycemia, hyperuricemia and hyperlipidemia.²²

Calcium pyrophosphate deposition disease or pseudogout (CPPD)

Pseudogout is characterized by deposition of CPPD crystals in the synovial structures resulting in inflammatory arthritis. Radiological findings include evidence of chondrocalcinosis and positive birefringent rhomboid-shaped crystals. Its prevalence in diabetics varies from 8–73%.²² It has been proposed that control of hyperglycemia in diabetic patients does not alter the frequency or severity of recurrent attacks of CPPD arthropathy.²³ But other workers have shown that diabetics have no association with CPPD.²⁴

Scleroderma

It is characterized by skin changes in the form of thickening, induration and infiltration. It mimics scleroderma. But it involves upper back while scleroderma affects the extremities. Secondary scleroderma is not associated with Raynaud's phenomena or antinuclear antibodies. Treatment goal is strict glycemic control.

Dupuytren's contractures (DC)

It is characterized by thickening and shortening of the plantar fascia, palmar or digital nodules leading to contractures in flexion of the affected finger. Usually the middle and ring fingers as well as hand are frequently involved bilaterally.²⁵

The prevalence of DC in diabetic patients varies from 20–63% as compared to 13% in nondiabetics.^{6,26,27} DC has close association with poor glycemic control, presence of microvascular complications and disease duration.²⁸ LJM and DC may occur together in the same patient.²⁹ Treatment of DC includes adequate glycemic control, physiotherapy and topical intralesional steroid injection while surgery is indicated for refractory cases. However surgery can lead to generalized hand stiffness.³⁰ So in such cases, conservative measures are recommended.

Carpal tunnel syndrome (CTS)

It is a painful, neuropathic disorder characterized by compression of the median nerve resulting in paresthesia over cutaneous distribution of thumb, index, middle and lateral half of ring fingers. It is a

form of entrapment neuropathy which is often worse at night.³¹ Its prevalence is 20% in diabetics and 75% in those with LJM.³² It is more common in females than males. It has close association with age and duration of diabetes.³¹ Treatment is conservative and surgery. The conservative therapy includes splinting, steroids, physiotherapy, analgesics and vitamin B6 supplementation.³³ Surgical treatment is indicated in those patients who fail to respond to conservative measures.³⁴

Trigger finger or stenosing flexor tenosynovitis

It typically presents as fingers locked in flexion, extension or both. It is caused by fibrous tissue proliferates in the tendon sheath resulting in limitation of normal movement of the tendon. It more commonly involves the thumb, third or fourth finger.³⁵ It's prevalence in diabetics varies from 5–36% and 2% in nondiabetics.³⁶ It is associated with greater duration of disease and not age and glycemic control.³⁷ Treatment includes use of nonsteroidal anti-inflammatory drugs and corticosteroid injection into tendon sheath and in severe cases, surgical treatment.³⁸

Frozen shoulder syndrome

It is also called as adhesive capsulitis of the shoulder or obliterative arthritis. It typically presents as complete progressive painful limitation on active and passive mobility of the shoulder especially abduction and external rotation.³⁵ It is associated with many other conditions including shoulder trauma as well as cerebral, cardiac and respiratory conditions. The natural history of the disease is characterized by three phases — painful, adhesive (stiffness) and recovery (resolved).³⁹ Its prevalence in diabetics varies from 10–29%.^{40,41} Increased prevalence of shoulder calcification has been noticed in those patients with longer duration of disease and treatment with insulin.⁴² The joint capsule becomes thickened and adherent to the head of humerus in case of idiopathic adhesive capsulitis, thus reducing the volume of glenohumeral joint. Treatment includes analgesics, physiotherapy, corticosteroid injection into the glenohumeral joint and subacromial bursa and kineto-therapy.⁴³ In refractory cases where above conservative measures fail, surgery is indicated.

Diabetic muscle infarction (DMI)

It is a rare complication of diabetes mellitus. It typically presents as acute onset of muscle pain and swelling involving thigh muscle in 80% of cases with palpable mass. But it may involve calf muscles and muscles of upper limb. Recurrence may occur in the same or different group of muscles with mortality rate of 10% due to macrovascular complications.⁴⁴ More than half of the patients had type 1 diabetes mellitus with a mean duration of 15 years.⁴⁵ There is no specific laboratory marker, but creatine kinase levels are found to be high only in few patients. Regarding radiological investigations, MRI reveals intense swelling on T1 weighted images and different hyperintensity on T2 weighted images of the involved muscle with features of subfacial and subcutaneous edema.⁴⁵ Muscle biopsy is indicated in undiagnosed atypical cases not responding to anti-inflammatory or antiplatelet treatment.⁴⁷ The exact etiology of this condition is not known but proposed mechanisms include reperfusion injury following muscle ischemia, endothelial dysfunction, hypercoagulability state and involvement of fibrinolytic system.⁴⁸ Differential diagnoses include myositis, tumor, adverse effect of simvastatin, venous thrombosis and ruptured Baker's cyst. Treatment is adequate glycemic control, antiplatelet drugs, antiinflammatory drugs etc, but no randomized controlled trials have been done yet.⁴⁹

Diabetic amyotrophy

It is characterized by burning, severe aching and lancinating pain in the hip and thigh, followed by weakness and wasting of the muscles with marked weight loss. It has correlation with poor diabetic control in 50% cases. EMG studies reveal neurogenic lesion in the lumbosacral roots, plexus and peripheral nerves.⁵¹ The most likely mechanism for this condition are inflammatory immune-mediated and vascular radioculoplexopathy.⁵² Treatment includes immunosuppressive therapy with cyclophosphamide and methylprednisolone in addition to good glycemic control with marked recovery in the majority of patients.⁵³ But many workers have reported that immunosuppressive therapy has no role.⁵⁴

Diffuse idiopathic skeletal hyperostosis (DISH)

It is also called Frostier disease and it is characterized by ossification of the ligaments and entheses and is especially associated with Type 2 DM. Other associated conditions include dyslipidemia, hyperuricemia and metabolic syndrome.⁵⁵ It typically presents as pain, snuffles, dysphagia, airway obstruction, radioculopathy with susceptibility to spinal fractures after minor trauma. Frequently involved areas of the spine are cervical and lumbar segments. The diagnosis of DISH is mainly based on radiological findings.

The criteria forwarded by various workers include evidence of symmetric peripheral enthesopathy and ossification along with anterolateral aspect of the two or more adjacent vertebral bodies.⁵⁶ Medical therapy includes use of NSAIDs, physiotherapy and control of associated metabolic disorders.

Osteoporosis

The association of diabetes with osteoporosis is controversial.⁵⁷ Diabetic patients have low bone metabolism, reduced bone formation and reduced bone resorption. These findings are due to low levels of insulin and IGF-1 in type 1 DM but reduced bone formation in type 1 and type 2 DM, is due to accumulation of advanced glycation end products (AGES). Bone mass is decreased and there is increased risk of fracture.⁵⁹

Reflex sympathetic dystrophy and complex regional pain syndrome (CRPS)

Typically it presents with allodynia, burning pain and hyperalgesia with marked autonomic features in the form of local edema, altered sweating and skin color.⁶⁰ It is of two types — CRPS-1 (reflex sympathetic dystrophy) and CRPS-2 (causalgia) depending upon absence or presence of documented nerve injury respectively.⁶¹ The International Association for Study of Pain (IASP) 1994 has laid down certain diagnostic criteria for CRPS type 1⁶² which includes

- (a) Type 1 is a syndrome which occurs after an initiating noxious event.
- (b) Spontaneous occurrence of pain in the absence of an external stimulus, allodynia or hyperalgesia

which is not confined to the location of a single peripheral nerve.

- (c) Evidence of edema of skin, decreased blood flow or abnormal sudomotor (alteration in sweating) activity.
- (d) Conditions causing pain and dysfunction to be excluded.

Although these criteria are nonspecific, they are widely reported in the literature.⁶³

Conclusion

Diabetes mellitus is associated with numerous musculoskeletal manifestations caused by long term metabolic derangements of diabetes mellitus and poor glycemic control. The upper limb (hand and shoulder) are most commonly involved. Identification and treatment of these complications in the form of pharmacotherapy, diet and physiotherapy are important in order to improve the quality of life of diabetic patients and thereby reducing the frequency and severity of complications.

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