Clinical Appearance and Treatment of Adhesive Capsulitis in Diabetes

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Diabetes mellitus is a diverse disease affecting 12 million Americans and presenting in multiple organ systems (1). Long-term complications of diabetes include alterations in connective tissue that occur as a result of changes in glucose homeostasis. These changes affect the extracellular matrix and may lead to significant dysfunction in a myriad of structures, such as blood vessels and skin. Although the etiology is most likely multifactorial, several studies have shown increased nonenzymatic alycosylation of collagen type-II fibers in the presence of high blood glucose levels (2, 3). This glycosylation leads to enhanced cross-linking among collagen molecules, which renders them more resistant to enzymatic degradation and may play a role in the contracture syndromes. Dupuytren's disease is an example of a contracture syndrome of the soft tissues of the palm with a well-established relation to diabetes. In this article, we present another contracture-type syndrome, adhesive capsulitis, which is a chronic complication of diabetes.

Definition and Risk Factors

Adhesive capsulitis, also known as frozen shoulder, refers to a pathologic condition of the shoulder of unknown etiology in which the patient presents with a gradual loss of motion in the shoulder joint. The decrease in mobility is due to a fibrotic thickening of the joint capsule with adherence to the humeral head, resulting in decreased joint volume. Tenderness and diffuse inflammation often accompany this contracture. In addition, this condition may lead to hyperhidrosis of the hand in the "shoulder-hand syndrome" (4).

Adhesive capsulitis has several risk factors, including female gender, long duration of diabetes symptoms, age older than 40 years, trauma, prolonged immobilization, thyroid disease, cardiovascular disease, and autoimmune disease in addition to diabetes (5–12). Adhesive capsulitis has a prevalence of 2% in the general population, or a little more than five million people. The prevalence of adhesive capsulitis in diabetes has been reported at 10.5% to 29% (5, 7). Approximately 20% to 30% of patients with adhesive capsulitis will develop the syndrome in the contralateral shoulder (10), and about 70% are women. Viral initialization and hormonal changes during the perimenopausal years may also play a role in its pathogenesis.

Historic Background

The term "adhesive capsulitis" was coined in 1945 when Neviaser (13) first documented changes in the synovium and subsynovium in a cohort of his patients with shoulder pathology. Its link to diabetes was revealed in 1972, when Bridgman (7) conducted a prospective study of 800 diabetic patients and 600 nondiabetic patients. Eighty-six (10.8%) of the people with diabetes and 14 (2.3%) of the nondiabetic controls were found to have adhesive capsulitis. Bridgman (7) also discovered that the incidence of adhesive capsulitis correlated with the duration of diabetes symptoms. In addition, 36 patients (4.5%) in the diabetic group had both shoulders affected versus 3 (0.5%) in the nondiabetic group. The author advocated diabetes screening in patients who present to their physicians with unilateral and especially bilateral frozen shoulder (7). Furthermore, people with Type 1 diabetes were found to have a greater predisposition to adhesive capsulitis than those with Type 2 diabetes (14).

Histologically, this disease is characterized by synovial inflammation followed by capsular fibrosis and collagen deposition (15–19). Rodeo and associates (18) showed the involvement of cytokines in the pathogenesis of adhesive capsulitis. Specifically, higher concentrations of transforming growth factor beta, platelet-derived growth factor, and hepatic growth factor have been isolated in the synovium and shoulder capsule of patients with adhesive capsulitis. These cytokines have been associated with other inflammatory and fibrotic sequelae in the body and are presumed to have similar functions in adhesive capsulitis.

Adhesive capsulitis can be divided into several stages. Hannafin and colleagues (10, 20) correlated the arthroscopic findings of adnesive capsulitis, as described by Neviaser and coworkers (16, 21), with the histologic and clinical findings. These stages are not discrete, but are rather reference points within the continuum of this disease. Proper diagnosis and staging have significant implications in the course of treatment and prognosis for the patient.

Diagnosis and Staging

Although the etiology of adhesive capsulitis is still unknown, recent studies have elucidated the pathophysiology of this condition, enabling clinicians to make more confident diagnoses. Adhesive capsulitis can be grouped into two major categories: primary, idiopathic adhesive capsulitis; and secondary adhesive capsulitis with known intrinsic or extrinsic origins. The pathogenesis of adhesive capsulitis is progressive, with a painful loss of range of motion (ROM) in the shoulder joint. There are four stages: initialization stage, freezing stage, frozen stage, and thawing stage. These are outlined in Figure 1.

Primary adhesive capsulitis. The course of primary adhesive capsulitis insidiously limits the patient's motion and prevents him from performing normal activities of daily living, especially activities with the arm overhead, abducted, or rotated internally or externally. Pain and inflammation in the shoulder can discourage patients from daily activities via reflex inhibition, further accelerating loss of motion. Conversely, forced activity despite pain and inflammatory symptoms can lead to subacromial impingement within the glenohumeral joint. After a period of time, the patient's pain usually diminishes, but the shoulder remains extremely stiff with severe limitations in ROM.

Secondary adhesive capsulitis. Secondary adhesive capsulitis has been associated with protease-inhibitor treatment. In a study of 12 patients treated with matrix metalloproteinase inhibitors for inoperable gastric cancers, 6 experienced a frozen shoulder or Dupuytren-like syndrome (22). Similarly, a recent report of eight patients who developed

FIGURE 1.

STAGES OF ADHESIVE CAPSULITIS

STAGE 1: INITIALIZATION STAGE

Duration of symptoms: 0 to 3 months

PE: Pain with active and passive ROM; limitation of forward flexion, abduction, internal rotation, external rotation

EUA: Normal or minimal loss of ROM

Arthroscopy: Diffuse glenohumeral synovitis

Histology: Hypertrophic, hypervascular synovitis; inflammatory-cell infiltrates; normal underlying capsule

STAGE 2: FREEZING STAGE

Duration of symptoms: 3 to 9 months

PE: Chronic pain with active and passive ROM; significant limitation of forward flexion, abduction, internal rotation, external rotation

EUA: ROM essentially identical to ROM when patient is awake

Arthroscopy: Diffuse, pedunculated synovitis Histology: Hypertrophic, hypervascular synovitis with perivascular and subsynovial scarring; fibroplasia and scar formation in the underlying capsule

STAGE 3: FROZEN STAGE

Duration of symptoms: 9 to 14 months

PE: Minimal pain except at extremes of ROM, significant limitation of ROM with rigid end point

EUA: ROM identical to when patient is awake

Arthroscopy: No hypervascularity, fibrotic synovial remnants, thick capsule with diminished capsular volume

Histology: Burned-out synovitis without significant hypertrophy or hypervascularity, dense scar formation

STAGE 4: THAWING STAGE

Duration of symptoms: 15 to 24 months

PE: Minimal pain, progressive improvement in ROM

EUA: Same as stage 3

Arthroscopy: Same as stage 3 with some cellular remodeling

Histology: Same as stage 3 with some cellular remodeling

PE indicates physical examination; EUA indicates examination under anesthesia; ROM indicates range of motion. Adapted from *Clin Orthop* Mar(372):95–109, 2000.

adhesive capsulitis of the shoulder secondary to indinavir treatment for human immunodeficiency virus infection implicated protease inhibitors as a possible initiating mechanism (23). Such treatments may shift the equilibrium of the glenohumeral synovium away from resolution of adhesions and toward the inflammatory and fibrotic processes inherent to this condition. Stage 1 disease. The diagnosis of adhesive capsulitis is made primarily from the history and physical examination after other causes of pain and loss of ROM have been eliminated. In stage 1, patients present with tenderness of less than 3 months' duration. Pain is elicited at the endpoints of ROM, and the shoulder is described as achy at rest. Since the initiation of the symptoms, patients usually report gradual loss of motion, particularly of internal rotation, forward flexion, abduction, and external rotation. Palpation of the anterior and posterior capsule elicits these pain symptoms, which may radiate to the insertion of the deltoid. Pain at night and at rest is also a common complaint. Injection with a local anesthetic allows a significant improvement in ROM and is diagnostic of stage 1 adhesive capsulitis. At this point in the natural history of the disease, the symptoms are due to inflammation within the synovium of the shoulder rather than a contracture syndrome. Arthroscopy and biopsy reveal a hypervascular synovitis with an influx of inflammatory cells.

Evaluation and documentation of active and passive ROM in the isolated glenohumeral joint are important for establishing reference points for later assessment of progression of the disease and efficacy of treatment. We advise that the following measurements be obtained actively and passively: forward flexion, abduction, internal rotation (highest spinous process on the back), and external rotation (with the elbow flexed 90°). Cervical spine examination should also be conducted. Workup should include routine x-rays of anteroposterior views in internal and external rotation, axillary views, and outlet views.

Radiographs are important for excluding other pathologic processes such as glenohumeral arthritis, glenoid or humeral fracture, calcific tendinitis, and osteopenia. Patients with stage 1 adhesive capsulitis have films that are essentially negative, reflecting a soft-tissue mechanism rather than an osseous one. Other soft-tissue pathologies that may mimic the symptoms of adhesive capsulitis, such as subacromial impingement, acute or chronic rotator-cuff defects, and labrum tears, can be ruled out with magnetic resonance imaging (MRI). MRI usually shows increased blood flow to the synovium in adhesive capsulitis. However, MRI is not routinely recommended for the diagnosis of adhesive capsulitis.

Stage 2 disease. Progression of the aforementioned process leads to stage 2 adhesive capsulitis. At this juncture, the symptoms have been present for 3 to 9 months, with continued loss of ROM. When a patient is injected with a local anesthetic during this stage, pain is alleviated but ROM improves minimally. The lack of improvement in ROM is a result of decreased capsular volume due to the chronic inflammatory condition in the joint space. Arthroscopic and histologic evaluations reveal a dense, hypervascular synovitis with perivascular scar formation, collagen deposition, and fibroplasia without inflammatory infiltrates. This marks the conversion of adhesive capsulitis from its inflammatory stage to a fibrotic process. X-rays of the patient in this stage reveal decreased joint space, particularly in the axillary recess. Stage 3 disease. These sequelae continue in stage 3, when patients present with marked stiffening of the shoulder as well as substantial loss of ROM. At this stage, pain has been present for 9 to 14 months, with some variability in the symptoms. In general, an extremely painful phase typically resolves spontaneously, but stiffness and loss of ROM persist. Injection with local anesthetics and examination under anesthesia reveal no change in ROM, indicating an intra-articular loss of joint space as a consequence of the capsular fibrosis. Arthroscopic and histologic evaluations at this stage are relatively unremarkable, with some synovial thickening but no hypervascularity or inflammatory infiltrates. Stage 4 disease. In stage 4, there is a gradual recovery of ROM because of cellular remodeling of the capsule, with increased shoulder motion. At this stage, the pain and active fibroplasia in the shoulder joint have completely subsided. Consequently, the patient must recover ROM in the shoulder via strength and conditioning exercises. Associated diseases. Several studies have

associated adhesive capsulitis with other syndromes. Increased rates of Dupuytren's disease, tenosynovitis, carpal tunnel syndrome, and "shoulder-hand syndrome" have been reported in the presence of adhesive capsulitis and may reveal a predisposition in certain individuals to other contracture-type conditions (4, 6, 7, 15, 24). Other studies have provided evidence that adhesive capsulitis is associated with retinopathy, but not with neuropathy or macroproteinemia (5, 7, 14). We believe that when a patient presents with adhesive capsulitis, he or she should be screened for other contracture syndromes, particularly of the hand. Similarly, early signs of retinopathy should be evaluated.

Treatment

Treatments for adhesive capsulitis include benign neglect, physical rehabilitation, intraarticular corticosteroid injections, distention arthrography, joint manipulation, and surgical release of the capsule of the glenohumeral joint. There has been a wide spectrum of opinions regarding treatment of this disease, with some clinicians favoring conservative treatments and others favoring more aggressive interventions (10, 24). Although treatment of this disease is still controversial because of drawbacks of each of the interventions, we believe that proper staging of this disease is paramount for establishing effective treatment guidelines, which are outlined in Figure 2.

General measures. Throughout the course of treatment, patients with pain and limited ROM are given nonsteroidal anti-inflammatory drugs (NSAIDs). Furthermore, an intraarticular injection of an analgesic may have diagnostic and therapeutic benefits. Early treatment with a corticosteroid injection is advocated because it can obliterate the synovitis, circumventing the subsequent fibrosis inherent to this disease. The use of specific cytokine inhibitors to slow the chemical engine of this disease is another area under current investigation.

Patients should also be placed in a supervised rehabilitation program to restore ROM, attenuate pain and inflammation, and reestablish normal glenohumeral function. The tenderness perceived by the patient often prevents the clinician from reaching an end point to ROM positions. Frequently, the resting position of the humeral head has moved

FIGURE 2.

REHABILITATION OF ADHESIVE CAPSULITIS

STAGE 1: INITIALIZATION STAGE

Goal: Interrupt inflammation and pain cycle Treatment: Education (resting position, postural correction), activity modification, NSAIDs, corticosteroid injection, ROM exercises (joint mobilization, gentle physiologic movement, continuous passive movement, continuous passive motion, hydrotherapy), closed-chain scapular stabilization, home-exercise program

STAGE 2: FREEZING STAGE

Goal: Decrease pain and inflammation, minimize capsular adhesions and restriction of ROM

Treatment: NSAIDs, corticosteroid injection, ROM exercises in the inferior and posterior directions, active exercise in the plane of the scapula, training of scapular muscles, homeexercise program

STAGE 3: FROZEN STAGE & STAGE 4: THAWING STAGE

Goal: Increase ROM

Treatment: Possible surgical intervention and manipulation, aggressive stretching (proprioceptive neuromuscular facilitation; soft-tissue mobilization; low-load, prolonged stretch), modalities to promote relaxation and tissue extensibility and reduce discomfort, strengthening to reestablish scapula force couples, home-exercise program

NSAID indicated nonsteroidal anti-inflammatory drug; ROM indicates range of motion. Adapted from *Clin Orthop* Mar (372): 95–109, 2000.

anteriorly because the patient has adopted an adducted, internally rotated position in response to the pain and inflammatory symptoms.

Stage 1 disease. In patients with stage 1 adhesive capsulitis, the goal of treatment is to retard progression of the disease caused by the painful synovitis. Activity modification is recommended to limit the tenderness that can initiate the cycle. Pain is attenuated with NSAIDs, other analgesics, cryotherapy, transcutaneous electrical nerve stimulation, and galvanic stimulation. Therapies to reduce inflammation include NSAIDs, cryotherapy, iontophoresis, phonophoresis, and local corticosteroid injection when appropriate. Relaxation of the muscles and shoulder joint is

achieved with moist heat and ultrasound therapies. Hydrotherapy is also advocated to provide resistive exercise, promote good biomechanics, and create a biofeedback effect.

Helpful exercises include closed-chain motions, where the distal aspect of the limb is fixed. Muscles that stabilize the scapula should be strengthened to promote a stable base for distal mobility. ROM can be improved through pendulum and passive exercises. Stage 2 disease. In stage 2 adhesive capsulitis, pain is usually elicited at the extremes of ROM. At this juncture, limitation in external rotation is most notable, with a rigid end point as a result of the fibroplasia. As in stage 1, the goal of therapy is to reduce the cycle of pain and inflammation. Passive shoulder movements are advocated to restore normal motion of the glenohumeral joint and reestablish joint space. Frequent ROM exercises including pendulums, cane exercises, and "end-ROM mobilization techniques" (25) are advised to improve internal and external rotation.

Stages 3 and 4 disease. Patients with stages 3 and 4 adhesive capsulitis often report a resolution of their painful symptoms, but are left with an extremely stiff shoulder with abnormal biomechanics. Intra-articular corticosteroid injection is contraindicated at this point because the inflammatory stage of the disease, in which such treatment would be most efficacious, has passed. We advise that treatment options be customized to individual patients and their particular degree of glenohumeral dysfunction.

The risks and benefits of surgical intervention versus continued physical rehabilitation must be weighed. The primary goal at this stage of the disease is to restore ROM through aggressive stretching beyond the patient's active ROM. An active warmup encourages blood flow to the area of interest. A protracted, low-load stress may increase the plastic deformation of the soft tissue of the capsule and encourage an increase in ROM. Conversely, quick and large forces lend to elastic deformation and a return to the prestretch state. Techniques may include proprioceptive neuromuscular facilitation, particularly mobilization of the subscapularis and pectoralis minor; heat (in the form of ultrasound or hot, moist cloths) to promote muscle relaxation; and cryotherapy to reduce tenderness after rehabilitation exercises.

The benefits of physical therapy are variable. Most patients report a significant improvement by 3–4 months, but others have symptoms that may even progress. Approximately 10% of patients have long-term problems with adhesive capsulitis (26). Treatments in patients refractory to physical therapy include continued physical rehabilitation, closed manipulation, arthroscopy, or capsular release and manipulation. More aggressive intervention is warranted in patients with persistent pain, stiffness, and loss of function for at least 1 year without improvement despite conventional conservative treatments.

Closed manipulation and arthroscopic release constitute the current surgical treatment options for adhesive capsulitis. During this process, the restricting soft tissue is physically stretched and torn as motion is restored in the entire ROM.

Arthroscopy should be performed before manipulation to rule out persistent synovitis, which could be excised without performing the manipulation. In addition, we advocate arthroscopy first to rule out intra-articular pathology and avoid fluid extravasation into the tissues as a result of manipulation. Arthroscopy is also useful in detecting concomitant pathologies, such as rotator-cuff or labral defects or subacromial impingement, and in inspecting the joint space and synovium. Once other pathologies have been excluded, arthroscopy, capsular release, and manipulation are performed.

The sequence of manipulation is as follows: forward flexion, extension, abduction, and internal and external rotation. Following manipulation, an arthroscopic capsular release is performed with the use of an electrocautery device and a motorized shaver. The capsular scar caused by the fibroplasia is divided, removing the most prominent restriction to ROM. The postoperative protocol entails aggressive ROM and stretching exercises, continuous passive motion, treatment for pain and inflammation, and hydrotherapy. Several studies have shown that arthroscopic release for refractory adhesive capsulitis is an appropriate intervention, producing significant increases in ROM compared with the preoperative state (27–29). These studies showed that patients with diabetes did worse initially, but the ultimate outcomes were comparable in patients with and without diabetes.

Discussion

In general, adhesive capsulitis is a self-limited disease with a clinical history involving a painful loss of ROM in the shoulder of several months' duration and a physical examination confirming painful, restricted motion. Upon initial examination, ROM should be evaluated and documented, and x-rays should be obtained to exclude other pathologies such as glenohumeral joint arthritis and fracture. In fact, the hallmark of this disease is loss of external rotation without evidence of glenohumeral arthritis on x-ray.

Patients should be treated with NSAIDs, corticosteroid injection, a supervised physicalrehabilitation program, and, if refractory to these treatments, closed manipulation and surgical capsular release. Staging of this disease is important when choosing treatments, and we emphasize that the stages represent a dynamic continuum rather than separate entities. Education of patients and detailed instruction about the course of the disease as well as rehabilitation goals are strongly advocated to increase compliance. Early detection, proper staging, and appropriate treatment can allow diabetic patients to avoid the painful and disabling sequelae that can appear in this disease.

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