Upper-Extremity Pain Disorders in Breast Cancer

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Upper-extremity pain is a common and debilitating problem for patients with breast cancer. Although there is considerable literature describing symptoms, little is available on the specific disorders responsible for pain and debility in these patients. Cervical radiculopathy, brachial plexopathy, neuropathy, rotator cuff tendonitis, adhesive capsulitis, epicondylitis, postmastectomy syndrome, swelling, and bone metastases are among the common disorders responsible for upper-extremity pain in breast cancer patients.

Overall Article Objective: To discuss common upper-extremity pain disorders in patients with breast cancer.

Key Words: Brachial plexopathy; Breast cancer; Electrodiagnosis; Pain; Radiculopathy; Rehabilitation.

UPPER-EXTREMITY PAIN DISORDERS are common in patients with breast cancer. Arm morbidity affects as many as 7 in 8 women after treatment for breast cancer.[1] Although many studies have focused on pain and clinical signs such as arm edema and restricted shoulder motion after breast cancer treatment, little information is available concerning the specific etiologies of pain and musculoskeletal disorders encountered in this population.[2] This review discusses several of the most common upper-extremity pain disorders encountered in breast cancer patients. An expanded list is presented in appendix 1.

COMMON PAIN DISORDERS

Cervical Radiculopathy

Cervical radiculopathy is common in the general population and may be encountered in breast cancer patients during any phase of their disease. Radiculopathy may present as pain, paresthesias, numbness, or weakness of the shoulder, arm, and/or hand. Upper cervical radiculopathy (C5 or C6) commonly radiates pain to the shoulder and upper arm and weakens the rotator cuff muscles, biceps, and deltoid. Shoulder pain and rotator cuff weakness may contribute to shoulder impingement and secondary adhesive capsulitis. Lower cervical radiculopathy (C8 or T1) may weaken the intrinsic hand muscles, resulting in decreased dexterity. Pain and paresthesias in the hand may be caused by nerve root dysfunction at any level and may mimic plexopathy or neuropathy. Symptomatic radiculopathy and other peripheral nervous system disorders can develop or worsen during or after treatment with neurotoxic chemotherapeutic agents.[3]

More than 90% of spinal cord compressions, including those at cervical levels, present with localized pain.[4] Radiculopathy as an early sign of spinal cord compression is relatively uncommon in the cervical spine but may result from tumor-related neural foraminal stenosis or epidural disease. Practitioners should quickly obtain imaging when cancer patients present with worsening neck pain or symptomatic radiculopathy.

Treatment of cervical radiculopathy depends on its etiology. Much of the cervical radiculopathy encountered in patients with cancer is unrelated to cancer or its treatments. Cervical spine magnetic resonance imaging (MRI) with and without gadolinium is generally indicated to exclude spinal metastases, epidural disease, and leptomeningeal disease (meningeal carcinomatosis). Electrodiagnostic testing is often useful in localizing the root level affected and for excluding disorders such as brachial plexopathy and peripheral neuropathy. The presence of spinal metastases does not automatically confirm that the tumor is the cause of radiculopathy. As in all radiculopathy, anatomic congruence, as evidenced by compression of a nerve root in the distribution of a patient's clinical signs and symptoms, should be sought.

Non–cancer-related cervical radiculopathy can be treated nonoperatively with physical therapy (PT), anti-inflammatory drugs, and nerve-stabilizing agents such as gabapentin. Malignant radiculopathy can respond to similar interventions but may also require chemotherapy, external beam radiation, or surgery. PT and occupational therapy (OT) can improve upper-extremity strength, dexterity, coordination, activities of daily living, and shoulder range of motion (ROM) and decrease neck spasms even when symptoms are caused by cervical metastasis. In the absence of mechanical instability, significant epidural disease (which could result in spinal cord compression), or progressive neurologic deficits (an indicator of spinal cord or nerve root compression), therapeutic activities including active and passive ROM exercises are generally safe. Deep-heating modalities, although contraindicated in primary tumors, are unlikely to worsen already metastatic disease and should be used where clinically beneficial. Treatment of insensate or irradiated skin is often necessary and should be done with caution. The addition of opioid medications may be necessary when pain control is not satisfactory with the aforementioned medication classes.

Brachial Plexopathy

In contrast to cervical radiculopathy, brachial plexopathy is rare in the general population and unlikely to be seen at diagnosis in the breast cancer patient unless the disease is advanced. Most brachial plexopathy seen in patients with breast cancer results from local tumor invasion or is a late complication of radiation therapy.[5]

The diagnosis of brachial plexopathy is often suspected on clinical grounds, especially when a patient has a known local recurrence of the cancer. Plexopathy resulting from radiation therapy may take months or years to develop. It is not always distinguishable from tumor recurrence and may coexist with it.

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An MRI of the brachial plexus with and without gadolinium is the test of choice to exclude an axillary recurrence. Positron emission tomography may also help to identify recurrence but does not provide as detailed anatomic information.

Electrodiagnostic testing helps distinguish plexopathy from radiculopathy and neuropathy. The presence of myokymia on needle electromyography suggests a radiation component to nerve injury but does not exclude recurrence. Both nerve conduction studies and needle electromyography are generally safe in patients with lymphedema.[6] In those patients with a history of recurrent cellulitis or marked anxiety about triggering or worsening lymphedema, we generally examine the ipsilateral cervical paraspinals and shoulder girdle muscles (ie, rhomboids and supraspinatus) unless it is anticipated that the electromyographic information from the distal extremity is likely to change our management.

Brachial plexopathy from either tumor recurrence or radiation is likely to progress. Chemotherapy, radiotherapy, or surgery may slow the progression of recurrent breast cancer. As in cervical radiculopathy, management with PT, OT, and pain medications such as nerve-stabilizing agents and opioids is useful in reducing pain and improving function. In patients who have progressed to "flail arm," a sling may be required to support the arm, and frequent passive ROM exercises may help prevent upper-extremity contractures.

Neuropathy

Many of the chemotherapeutics used to treat breast cancer produce neuropathy, a complication that is often responsible for upper-extremity pain. Taxanes are commonly used to treat breast cancer and can result in neuropathy.[7] Patients with preexisting neuropathy may be more likely to develop neuropathic signs and symptoms when treated with neurotoxic chemotherapy.[8] Oral glutamine, 10g orally 3 times a day for 3 days starting 24 hours after each chemotherapy treatment, may prevent some of the signs and symptoms of neuropathy in patients treated with paclitaxel.[9]

Chemotherapy-induced neuropathies typically present in a distal, symmetric distribution. Electrodiagnostic testing is indicated whenever a patient's neuropathic symptoms are atypical in presentation or distribution or when the symptoms develop more rapidly, are more severe, or occur at lower doses of chemotherapy than expected. Radiculopathy, median mononeuropathy, and other peripheral nervous system disorders are commonly found during electrodiagnostic testing in patients referred for signs and symptoms of chemotherapy-induced neuropathy.

Treatment of neuropathy is dependent on the type and severity of signs and symptoms. Nerve stabilizers are broadly beneficial in relieving positive symptoms such as pain and paresthesias but they will not alleviate numbness, weakness, or proprioceptive deficits. Nonsteroidal anti-inflammatory drugs (NSAIDs), tramadol, and weak opioids are often effective in the treatment of breakthrough pain. Severe neuropathic pain that cannot be managed with nerve stabilizers and adjuvant medications may require stronger opioids. PT may improve strength, coordination, proprioception, and endurance as well as alleviate pain, especially if other disorders, such as a compressive cervical radiculopathy, are contributing to symptoms. Treatment of patients with median mononeuropathy should also include a resting hand splint in a neutral position worn at night to prevent excessive and prolonged wrist flexion-extension during sleep.

Rotator Cuff Tendonitis

Rotator cuff tendonitis is common in the general population and is among the most common disorders seen in breast cancer patients. The precise pathogenesis of rotator cuff disease is controversial but is generally considered to be multifactorial and related to a combination of intrinsic and extrinsic factors.[10] One factor contributing to the development of rotator cuff tendonitis is impingement or shearing of the rotator cuff tendons between the coracoacromial arch and the humeral head. Many other factors may also contribute to impingement of the rotator cuff and, ultimately, the development of rotator cuff tendonitis in patients with breast cancer. Fatigue or failure of the dynamic stabilizers, rotator cuff, or scapular rotators can cause subtle instability of the glenohumeral joint, scapula dyskinesia, or anterior and superior subluxation—any of which may result in impingement of the rotator cuff.[11] One of the most important of these factors in breast cancer patients is weakness of the rotator cuff musculature. Cervical degenerative changes, metastases, or neurotoxic chemotherapy commonly damage the upper cervical (C5 and C6) nerve roots, resulting in rotator cuff weakness. Radiation to the cervical spine for metastatic disease and radiation that includes the rotator cuff muscles, nerves, or shoulder capsule may also play a role in the development of rotator cuff tendonitis. An association with lymphedema has been reported.[12]

Although MRI is considered the criterion standard for diagnosing rotator cuff tendonitis, the diagnosis is generally made on clinical grounds. The Hawkins, Neer, and supraspinatus impingement tests have good sensitivity and specificity.[13] Adhesive capsulitis may coexist with rotator cuff tendonitis and confound its diagnosis.

A subacromial injection should alleviate impingement signs acutely and help confirm the diagnosis. The injection also serves as at least a partial treatment for the rotator cuff tendonitis but should be combined with immediate PT or OT and NSAIDs. Residual neck and shoulder pain after resolution of impingement signs and symptoms generally indicates an upper-cervical radiculopathy and may benefit from the treatments previously described.

Adhesive Capsulitis

Also known as frozen shoulder, adhesive capsulitis is a complication that is very common in patients with breast cancer. Any disorder that causes restricted shoulder motion can cause synovitis and ultimately the capsular fibrosis of adhesive capsulitis. Local incisional pain from breast or axillary surgery, breast reconstruction, rotator cuff tendonitis, radiculopathy, local tumor recurrence, bony metastases, infection, radiation, and lymphedema commonly limit shoulder motion either voluntarily or subconsciously as a patient attempts to avoid painful maneuvers. Adhesive capsulitis can be painful even if no other disorders coexist. The diagnosis is made on the basis of restricted passive ROM at the glenohumeral joint. Motion may be restricted in all planes but external rotation and abduction are generally most limited.

The prognosis for recovery from adhesive capsulitis in a patient breast cancer depends largely on the phase of cancer treatment. Patients who develop adhesive capsulitis as a result of primary breast surgery generally have a good prognosis and often improve as their surgical pain resides. Treatment with NSAIDs, subacromial or intra-articular injections; therapy for ROM; and postural and strengthening exercises are generally adequate for complete recovery. Patients with coexistent disorders such as cervical radiculopathy and rotator cuff tendonitis underlying their adhesive capsulitis should have all disorders addressed simultaneously. Adhesive capsulitis secondary to disorders such as an axillary breast cancer recurrence generally have a worse prognosis. Aggressive pain control, including

subacromial injections, is appropriate in this setting to facilitate therapy to maintain or improve ROM.

Lateral Epicondylitis

Lateral epicondylitis is another common disorder among patients with breast cancer. Limitations in shoulder motion may cause patients to hyperextend the wrist during basic activities such as door opening. Repetitive hyperextension of the wrist as compensation may stress the extensor tendons and ultimately lead to lateral epicondylitis.

Pain is elicited by palpation over the origin of the extensor tendons or with resisted wrist and finger extension. Treatment includes rest, NSAIDs, PT with modalities and manual treatments, and perhaps steroid injections. A wrist splint in the neutral position may prevent wrist hyperextension. Forearm compression bands are also useful but are relatively contraindicated in patients with ipsilateral lymphedema, because they create a tourniquet effect and may worsen that condition. Injections to the area of the lateral epicondyle are generally safe, even in patients with lymphedema, so long as there is strict adherence to sterile technique and patients are carefully monitored for any signs of infection.

Postmastectomy Syndrome

Postmastectomy syndrome is a multifactorial disorder characterized by burning, stabbing, tightness, and aching in the axilla, medial upper arm, chest, and surgical scar; it is analogous to the stump and phantom pain experienced by extremity amputees. Injury to the intercostobrachial nerve is usually a major factor and can lead to numbness, paresthesias, and neuropathic pain involving the medial upper arm (intercostobrachial neuralgia). Shoulder ROM may be compromised because of pain, sensory loss, and radiation fibrosis resulting in adhesive capsulitis or rotator cuff tendonitis. Axillary dissection or breast reconstruction with implants after mastectomy can cause direct nerve injury at the time of surgery or progressive nerve compression as scar tissue develops.

As with other amputations, postmastectomy patients can experience phantom breast pain and sensation. Pain that is not typical of postmastectomy pain syndrome or progressive pain despite nonsurgical management should prompt evaluation for infection and tumor recurrence. Treatment generally involves therapy for ROM and skin desensitization, nerve stabilizers, and analgesics.

Edema

The upper extremity may show edema immediately after surgery or as a late complication; this condition is often associated with pain. Some degree of immediate postoperative swelling is expected and should resolve spontaneously. Persistent (more than a few weeks) or worsening swelling should prompt evaluation for seroma formation, wound infection, or skin/muscle flap necrosis. Late onset of upper-extremity pain and swelling in the postmastectomy patient can indicate cellulitis, deep vein thrombosis, recurrence of tumor, or lymphedema. Diagnosis and management of these conditions is discussed extensively elsewhere.[14] Lymphedema may predispose patients to a number of other musculoskeletal pain syndromes, including rotator cuff tendonitis, adhesive capsulitis, lateral epicondylitis, and de Quervain's tenosynovitis.[15]

Bone Metastases

Bone metastases occur in up to 70% of patients with advanced breast cancer.[16] The humerus is the most common upper-extremity site for bony metastasis, and pathologic fractures can result. Painful metastasis to the humerus may indicate fracture or impending fracture and should not be manipulated until treated with surgery or radiation. Nonfractured bone can be treated with palliative radiation therapy, chemotherapy, or both. Pharmacologic pain management using NSAIDs, opioids, bisphosphonates, and adjuvant therapies may be necessary. Judicious bracing may reduce risk of fracture and allow for non–weight-bearing functional activities in selected cases. Prophylactic surgical fixation of impending pathologic fractures is indicated if a patient remains symptomatic despite nonsurgical treatment or if the upper extremity is needed for weight bearing.

CONCLUSIONS

Upper-extremity pain disorders are common in breast cancer survivors and can occur at any time during the course of disease. The cause of pain in this population is multifactorial. Although much is known about the incidence of pain, lymphedema, and upper-extremity dysfunction in breast cancer survivors, more research into the specific causes, optimal treatment, and the prevention of pain in this setting is needed.

APPENDIX 1: COMMON UPPER-EXTREMITY PAIN DISORDERS IN PATIENTS WITH BREAST CANCER

- Radiculopathy
  - Leptomeningeal disease
- Plexopathy
- Neuropathy
  - Polyneuropathy
  - Mononeuropathy multiplex
  - Mononeuropathy
    - Median mononeuropathy (carpel tunnel syndrome)
    - Ulnar neuropathy
    - Radial neuropathy
- Myopathy
- Tendonitis
  - Rotator cuff
  - Bicipital
- Adhesive capsulitis
- Epicondylitis
- de Quervain's tenosynovitis
- Postmastectomy syndrome
  - Intercostobrachial neuralgia
  - Axillary pain (postsurgical)
- Edema
  - Postoperative swelling
  - Cording (thrombophlebitis)
  - Lymphedema
  - Deep venous thrombosis
- Complex regional pain syndrome
- Cellulitis
- Arthritis
- Metastases

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