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WINTER 2025



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Physiatric Approach to Pain in Breast Cancer



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Case Vignette

AP is a 65-year-old female who presents for left breast and chest wall pain. She has stage IIIA infiltrating ductal carcinoma of the left breast (estrogen receptor positive, progesterone receptor positive, and Her-2/neu negative), who was diagnosed 11 years ago. She had a modified radical mastectomy 11 years ago, completed chemotherapy (Docetaxel/Cyclophosphamide, paclitaxel) 10 years ago, and completed 60 Gray in 33 fractions of radiation therapy to the left chest wall 10 years ago. She is currently on Arimidex and tolerating it well for the last decade.

She reports constant tightness and intermittent spasms in her left chest wall, which have progressively worsened in the last 6-7 years. She reports spasms about 5-6 times per day that occur during overhead activities. She is left-handed and has learned to compensate with the right hand for most of her ADLs. She stopped gardening due to the frequency of her painful spasms.

She completed two courses of physical therapy focused on chest wall tightness with minimal improvement but does admit to lacking consistency with her home exercise program. She intermittently uses Naproxen as needed with little relief of her pain. She is seeking alternate treatment options at the UPMC Cancer Rehabilitation clinic for her worsening pain.

Epidemiology

According to recent American Cancer Society (ACS) data from 2023, breast cancer accounts for 31% of new diagnoses of cancers found in females and is estimated to be responsible for 15% of cancer-related deaths in the United States.¹ Furthermore, the World Health Organization estimated that globally, breast cancer led to 670,000 deaths.² In 2023, it was estimated that there would be 297,790 new cases of breast cancer in females and 43,170 estimated deaths.¹ However, it should be noted that mortality of breast cancer in females has been declining since 1989,

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which is associated with improvement in treatments and earlier diagnosis.¹ Risk factors for breast cancer include female sex, age, obesity, family history, age of menarche, tobacco use, alcohol use, and use of postmenopausal hormone therapies.² Oncologic treatments might be used independently or combined, which include surgery, radiation therapy, chemotherapy, hormonal therapy and/or immunotherapy.² These treatments can lead to undesirable short-term and long-term effects causing pain and weakness in the treated areas. A common concern for this patient population includes post mastectomy pain syndrome (PMPS), and the aim of this review is to learn musculoskeletal and neuropathic causes of PMPS in patients with breast cancer.

Diagnosis of PMPS

There are no clearly defined or commonly accepted diagnostic criteria for PMPS. Clinically, patients with any lingering chest wall/breast/shoulder pain months after surgery beyond the typical time frame for surgical healing can be considered to have PMPS. However, PMPS has previously been defined as persistent pain following breast surgery lasting greater than three months after surgical intervention.³ Notably, this is a diagnosis of exclusion after other causes of pain have been ruled out such as tumor recurrence or infection. PMPS has been characterized as a dull, burning or aching pain in the chest, breast, arm and axilla.³ According to Wisotzky et al, PMPS has a reported incidence of 20-70%.³ Some risk factors for developing PMPS include younger age, anxiety and/or depression,

axillary lymph node dissection, adjuvant radiation, severity of acute postoperative pain, and lower socioeconomic status.³ Younger patients are at increased risk of PMPS due to the likelihood of receiving more aggressive cancer treatments with heightened nerve sensitivity.

Clinical Evaluation

PMPS has several musculoskeletal and neuropathic etiologies.^{3,4} When approaching the evaluation of a patient with possible PMPS, a thorough review of their oncologic and pain history in combination with the physical examination is essential. Pertinent history includes onset of their symptoms, quality of pain, location of pain, duration of symptoms, any associated symptoms such as numbness, tingling or weakness, and any exacerbating and alleviating factors of the symptoms. It is also important to distinguish between breast pain and the presence of phantom pain or sensations following surgery. From an oncologic standpoint, it is important to identify the type of breast surgery performed, if the patient had an axillary lymph node dissection or sentinel node biopsy, how many lymph nodes were removed, and how many nodes were positive for metastatic disease. For example, removal of chest wall muscles in a radical mastectomy may negatively impact shoulder movements. Similarly, determining if a lymph node dissection was performed and if any lymph nodes were removed will help in determining the patient's risk of developing lymphedema post-surgery.

Table 1. Review of Clinically Relevant Breast/Chest Wall Musculature²²

Muscle	Proximal Attachment	Distal Attachment	Action	Innervation
Pectoralis major	Costal cartilage, sternum, clavicle	Intertubercular groove of humerus	Adduction and flexion of arm. Medial rotation of arm at shoulder	Medial and lateral pectoral nerves
Pectoralis minor	Ribs 3-5	Coracoid process of scapula	Protraction and depression of scapula	Medial pectoral nerve
Serratus anterior	Ribs 1-8	Medial border of scapula	Protraction and upward rotation of scapula	Long thoracic nerve
Latissimus dorsi	Ribs 10-12, Thoracolumbar fascia, Iliac crest, T7-L5 spinous processes	Intertubercular groove of humerus	Extension and adduction of arm	Thoracodorsal nerve
Supraspinatus	Supraspinous fossa of scapula	Greater tubercle of humerus	Abduction of arm	Suprascapular nerve
Teres minor	Lateral border of scapula	Greater tubercle of humerus	Lateral rotation of arm	Axillary nerve
Infraspinatus	Infraspinous fossa of scapula	Greater tubercle of humerus	Lateral rotation of arm	Suprascapular nerve
Biceps brachii	Supraglenoid tubercle of scapula (long head) and Apex of coracoid process of scapula (short head)	Radial tuberosity of humerus	Flexion of shoulder/arm, flexion of elbow, supination of forearm	Musculocutaneous nerve

Table 2: Breast Surgery Terminology²²

Types of Mastectomies	Breast Tissue Removal	Lymph Node Removal	Muscle Removal
Lumpectomy/Segmental mastectomy/Partial mastectomy	Abnormal tissue in the breast is removed	Sentinel node biopsy if indicated for biopsy	No
Total/Simple mastectomy	Whole breast tissue with a large ellipse of the skin, including the nipple and areola removed	Axillary lymph nodes typically not removed	No
Modified radical mastectomy	Whole breast tissue removed	Axillary levels I/II removed	Investing fascia removed, chest wall muscles preserved
Radical mastectomy	Whole breast tissue removed	Axillary lymph nodes levels I/II removed	Some chest wall muscles removed, including the pectoralis major and minor
Axillary lymph node dissection	Usually performed after sentinel node biopsy with varying levels of tissue removal	Axillary lymph nodes removed	No

If the patient underwent reconstruction surgery, donor sites for flaps should also be considered in the evaluation depending on the location of the patient's symptoms. For example, common flap sites include the transverse rectus abdominus muscle, latissimus, and deep inferior epigastric perforator.³ These regions may subsequently have reduced strength on examination. The mode, dose and location of radiation is important in the early identification of both acute and late radiation effects. Chemotherapies, hormonal therapies, and/or immunotherapies may also contribute to the patient's presentation. Premorbid cervical or shoulder musculoskeletal pathology which results in baseline pain and/or weakness can increase the risk of PMPS following cancer-directed treatments. Similarly, a brief psychosocial evaluation should be completed when there are concerns for untreated anxiety or depression that can heighten pain.^{3,4}

The physical examination should start with a skin examination of the breasts, chest wall, axilla and upper extremity looking for signs of infection, radiation skin changes, swelling, lymphedema, fluid-filled pockets, muscle atrophy, or scapular winging. The surgical incision site should be carefully evaluated for infection, seroma or neuroma. Thorough palpation to the affected musculature is necessary to assess for cording, taut bands/trigger points, or spasms that could be the source of pain. The primary muscles that can generate pain include the pectoralis, serratus anterior, latissimus dorsi, trapezius, supraspinatus, teres minor, infraspinatus, biceps brachii and rhomboids. Due to the location of the breast surgeries and radiation, these muscles are most often directly surgically manipulated or irradiated. See Table 1 for a summary of the origin, insertion, action and innervation of these muscles to better understand how such changes can impact the patient's function.

A complete shoulder examination is vital including passive and active range of motion (ROM), palpation of bony landmarks around the joint, and special tests. Strength, sensation and deep tendon reflexes of the bilateral upper extremities should be evaluated. Certain nerves may be more affected in breast surgeries, such as thoracodorsal, long thoracic, medial, and lateral pectoral nerves.³ Table 2 describes different breast surgeries and the structures that can be surgically removed. For example, the removal of chest wall muscles such as the pectoralis major and minor in a radical mastectomy significantly impacts shoulder function and will be evident on exam. Likewise, if the long thoracic nerve to the serratus or spinal accessory nerve to the trapezius are affected, then medial or lateral scapular winging may be noted, respectively. Surgical injury to the shoulder muscles and nerves can lead to scapular dyskinesia during scapulohumeral movements which may result in restricted ROM, strength loss or pain.

PMPS Differential Diagnosis

PMPS has several possible etiologies, most of which arise from musculoskeletal or neuropathic conditions that are summarized in Tables 3 and 4 on pages 4 and 5.

Musculoskeletal Causes

When considering musculoskeletal etiologies of PMPS, one of the most common causes is rotator cuff dysfunction, oftentimes preceded by shoulder impingement symptoms. In breast cancer patients, impingement can occur commonly as radiation fibrosis of the pectoralis major muscle causing tightening of the muscle and soft tissues; likewise, reconstruction can place stress at the pectoralis major attachment point. Both circumstances can result in a protracted, inferiorly positioned shoulder joint causing

narrowing of the subacromial space.^{5,6} Lymphedema or scar tissue involving the rotator cuff and chest wall muscles can further aggravate impingement due to functional overload of the ipsilateral limb.³ The exam can reveal pain in the anterior or anterolateral aspects of the shoulder, limited active ROM, and a positive Neer's, Cross-arm, Hawkins-Kennedy test, and/or painful arc test.⁵ The diagnosis is based on clinical evaluation but further imaging such as ultrasound (US) or MRI can be pursued to confirm shoulder pathology. Treatment is similar to rotator cuff dysfunction in the general population; most cases show improvement in ROM and pain with physical therapy focused on rotator cuff ROM, stretching, strengthening and scapulothoracic neuromuscular retraining. If conservative measures fail to improve symptoms, a subacromial corticosteroid injection can be considered if no metastases are confirmed radiologically.⁵

Adhesive capsulitis can occur from mastectomies and radiation causing tightening and fibrosis of the shoulder musculature, which can ultimately lead to severely restricted ROM of the entire shoulder girdle causing a contracted glenohumeral joint.^{5,7} Therefore, the exam reveals very limited ROM in both passive and active ROM, particularly with shoulder external rotation and abduction.⁵ Treatment includes physical therapy focused on manual therapy for tissue/joint mobilization^{5,8} and over-the-counter NSAIDs and acetaminophen as needed.⁷ If conservative measures fail, an intraarticular corticosteroid injection can be

considered if no malignancy is identified in the area. In refractory cases, surgical referral may be necessary for manipulation under anesthesia or capsular release.⁷

A significant portion of patients who receive radiation therapy can unfortunately face late radiation effects, which cause spasms from the fibrosis occurring months to years following completion of radiation therapy. Acutely after radiation, some patients may notice intermittent pain in the irradiated muscles. It is common that patients develop worsening tightness, pain and limited ROM several months to years post-radiation. Clinically, these patients typically complain of spasms or tightness as early as 4-12 months following radiation or in some cases, several years after radiation treatments.⁹ Radiation causes progressive fibrosis of any structure within the radiation field, which includes tissue, bone, ligament, nerve and/or vasculature. Radiation alone causes increased inflammation and a downstream influx of fibroblast production, which can cause unorganized firing of nerves and dystonic muscle spasms. Fibrosis itself can also cause tightening and shortening of muscles, tendons and ligaments which can lead to spasms.⁶ Patients are tender to palpation in the areas with the highest burden of spasms as well as an associated decreased ROM of the shoulder joint. Spasms are more commonly identified in the pectoralis major, latissimus dorsi, teres major and serratus anterior muscles. Skin changes associated with fibrosis include thickened, tight, and erythematous skin.

Table 3: Musculoskeletal Causes of PMPS

Diagnosis	Pathophysiology
Rotator cuff dysfunction	Impingement causing a protracted, inferiorly positioned shoulder joint can be caused by: <ul style="list-style-type: none"> – Lymphedema – Scar tissue – Radiation fibrosis to the pectoralis major – Reconstruction involving the pectoralis major^{5,6}
Adhesive capsulitis	Mastectomies and radiation cause fibrosis → protracted shoulder girdle muscles → contracted glenohumeral joint ^{5,7}
Radiation fibrosis/spasms	<ul style="list-style-type: none"> – Progressive fibrosis of tissue, bone, ligament, nerve and/or vasculature – Fibroblast production causes unorganized firing of nerves and dystonic muscle spasms. – Fibrosis causes shortening of muscles, tendons and ligaments leading to spasms.⁶
Axillary cording/Axillary web syndrome	Sclerosis of lymphatics and/or veins ¹²
Myofascial pain syndrome	<ul style="list-style-type: none"> – Muscle overuse – Pectoral tightness and scapular dyskinesia⁴
Capsular contracture	Physiological capsule can develop around breast implant which can become thick and fibrosed, leading to pain and contraction ¹³
Breast reconstruction	First phase involves tissue expansion (typically of the pectoralis major) which causes pain as it is stretched. The attachment points can be stressed which cause spasms. ⁶

Table 4: Neuropathic Causes of PMPS

	Pathophysiology
Phantom breast pain	Changes in central nervous system causes painful sensations of the removed breast or nipple ⁴
Intercostobrachial nerve (ICBN) pain	After axillary node dissection or mastectomies ¹⁷
Neurogenic thoracic outlet syndrome/pectoralis minor syndrome	Compression around the clavicle of the brachial plexus below the pectoralis minor, which can be shortened after surgery and fibrosed after radiation ²¹
Brachial plexopathy	<ul style="list-style-type: none"> – Compression from neurogenic thoracic outlet syndrome – Pectoralis minor syndrome – Radiation fibrosis – Metastatic lesion¹⁸
Cervical radiculopathy	Compression of cervical nerve roots can be worsened by radiation and systemic chemotherapies or direct compression from metastatic disease ²³
Intercostal neuromas	<ul style="list-style-type: none"> – Improper nerve repair following insult/injury to the nerve such as pressure, stretch, traction, ischemia, sharp transection, etc. – Can be found in scar tissue after mastectomies.^{6,19}

The key to preventing or minimizing the effects of radiation fibrosis is early mobilization after surgery. Once symptoms have begun, myofascial release and ROM are essential.⁸ Compliance with a daily home exercise program focused on ROM and stretching is key. Beyond physical therapy, interventions may include botulinum toxin injections and nerve blocks to the areas with muscle hyperactivity.¹⁰ In a retrospective review by Fu, et al, most breast cancer survivors who received onabotulinumtoxinA injections complained of muscle spasms or cramps ($p=0.0005$) pre-injection with 94% of injected patients reporting improvement in their pain level post-procedure. In this study, the median units were 100 units of onabotulinumtoxinA, and the most common muscles injected were the pectoralis and latissimus dorsi.¹¹ If pectoralis major and minor are mostly affected, PECS I and PECS II nerve blocks can be considered.⁶ PECS I is a type of nerve block between the pectoralis major and minor to block the medial and lateral pectoral nerves; PECS II additionally targets the intercostal, long thoracic and intercostobrachial nerves.

Axillary web syndrome, also known as axillary cording, can be seen in breast cancer patients. The etiology is due to sclerosis of lymphatics and veins of the axilla, which cause a taut cord in the axilla.¹² Cording leads to significant discomfort and restricted, painful ROM of the shoulder. This is a clinical diagnosis which tends to respond to physical therapy focused on myofascial release, soft tissue mobilization techniques, and gentle ROM of the cord. Cases may resolve spontaneously, and a “pop” can be noted by the patient.

Myofascial pain syndrome is observed in the breast cancer population. The etiology is thought to be related to muscle overuse but pectoral tightness and scapular dyskinesia after

cancer treatments are also implicated.⁴ Examination reveals taut bands or “trigger points” that are painful with compression, more commonly affecting the upper trapezius, levator scapulae, pectoralis major, latissimus dorsi and serratus anterior. Treatment includes therapy focused on myofascial release, stretching, scapulothoracic neuromuscular retraining, manual massage in conjunction with trigger point injections and dry needling with a local twitch response.^{4,7}

Following a breast implant, a capsule develops around the implant that helps to maintain the proper location. However, the capsule can become thickened and fibrosed leading to pain and contraction.¹³ Grading is based on the Baker classification system that assesses firmness of the breast, visibility of the implant, presence of pain and deformities.¹⁴ Treatment includes over-the-counter NSAIDs, acetaminophen and immediate referral to surgery for evaluation of a capsulectomy with removal and replacement of the implant.¹⁵

Neuropathic Causes

Neuropathic causes of PMPS can include phantom breast pain or sensation. Following various types of mastectomies, patients can develop painful phantom sensations in the area where breast tissue, nipple and/or areola were removed.⁴ Patients can report itching, tingling, pressure, or dysesthesias around the area of removed tissue.^{4,16} This is a clinical diagnosis that is made after other potential sources of pain are ruled out. Treatment includes physical therapy focused on desensitization techniques of the breast, nerve-stabilizing medications like gabapentin or SSRI/SNRI, lidocaine patch, or interventions such as nerve blocks, epidural injection or nerve stimulators.¹⁶

A common cause of PMPS is intercostobrachial neuralgia, which is a nerve that can be injured during an axillary lymph node dissection.¹⁷ Exam reveals pain and dysesthesias along the T1 and T2 dermatomal distributions, which provides sensation to the medial upper arm, axilla and lateral chest wall on the ipsilateral side¹⁷ with a possible Tinel's sign in the medial portion of upper arm.¹⁸ Treatment includes neuropathic medications, but some cases may require an intercostobrachial nerve block, which typically provides relief of symptoms.⁶ Intercostal neuromas can arise after the nerve is damaged from pressure, stretch, traction, or ischemia, oftentimes found in scar tissue after mastectomies.^{6,19} Affected nerves can be injured during the mastectomy and cause burning, shooting pain, and pain with palpation over the neuroma.²⁰ Imaging such as ultrasound may be helpful to visualize the neuroma if not evident on examination. Diagnostic nerve blocks are also utilized.^{4,19} If neuropathic medications and topical analgesic agents are not successful in relieving the pain, nerve blocks, surgical excision with autologous fat grafting, and targeted muscle reinnervation can be considered.⁴

One cause of neuropathic pain in PMPS is neurogenic thoracic outlet syndrome, which occurs when there is compression around the clavicle of the brachial plexus below the pectoralis minor, which can be shortened after surgery and fibrosed after radiation.²¹ On examination, there will be swelling and/or weakness of the ipsilateral upper extremity and atrophy of the intrinsic hand muscles. A positive Roo's test may be present, where the patient abducts and externally rotates their shoulder with the elbow at a 90 degree angle and the patient opens and closes their hand with reproduction of symptoms indicating a positive result.⁴ EMG/NCS of the upper limb is helpful in the diagnosis of neurogenic thoracic outlet syndrome.⁴ Furthermore, MRI of the brachial plexus can assess for compression and edema.¹³ Treatment includes stretching to the pectoralis muscle and strengthening of the scapular retractors to help relieve pressure. Severe cases may require surgical consultation for pectoralis minor tenotomy.⁴

In addition to neurogenic thoracic outlet syndrome, the brachial plexus can be compressed by radiation fibrosis or a metastatic lesion.¹³ Clinically, pain is typically acute in nature and involves the lower plexus in metastatic lesions compressing the plexus. In contrast, radiation-induced plexopathy is classically painless and involves the upper trunk. In such presentations, it is imperative to rule out metastatic spread with MRI or PET/CT. EMG/NCS can also

be used which may show myokymic discharges in radiation-induced plexopathy, while fibrillation potentials can be observed in metastatic plexopathy.^{4,18} Features that are more supportive of radiation associated myokymic discharges include localization to the brachial/lumbar plexus, myokymia discharges in more than muscle, and the presence of myopathic units accompanying the myokymic discharges.²⁰ Among radiation associated cases of myokymic discharges, there was no involvement in hand muscles.²⁰ Treatment for radiation-induced plexopathy is focused on strengthening of the weakened musculature and use of orthotics for functional support. Neuropathic medications are not needed typically in radiation-induced cases. If there is confirmed spread of the cancer to the plexus, the patient's oncology team should be notified immediately for further workup and cancer-directed treatments.

Case Vignette Outcome

Our patient AP revealed significant tenderness to palpation where she noted the greatest number of spasms, which were in the left pectoralis major and latissimus dorsi. Because of pain, she also had restricted shoulder abduction and flexion to about 100 degrees on the ipsilateral side. Her presentation was suspicious for PMPS resulting from radiation fibrosis of the involved musculature. AP had already completed two courses of physical therapy without improvement.

She received onabotulinumtoxinA injections to the left pectoralis major and latissimus dorsi muscles using a total dose of 60 units; 40 units into two locations in the latissimus and 20 units into area of the pectoralis. Education was also provided on compliance with daily home stretching and ROM exercises to optimize the effects from her neurotoxin injections. At her 4-week follow-up visit, AP reported improvement in her constant tightness by 50% and a reduction in spasm frequency to about three times per day, down from 5-6 spasms/day. Three months later, she underwent repeat onabotulinumtoxinA injections with up-titration injecting 50 units into each muscle. One month after her repeat injections, she reported an improvement of her constant pain from 8/10 intensity to 2/10 and a reduction of spasm frequency to 1-2 per day. Her pain relief lasted about 10 weeks after each subsequent injection cycle. She completed her home exercises regularly and had a significant reduction in pain with overhead activities including gardening.

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