Red flags, inflammatory conditions, and sinister shoulder pathology

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Introduction

Most musculoskeletal conditions involving the shoulder are benign and respond to a wait and watch approach or appropriate nonsurgical management. However, in a small proportion, symptoms that appear to be musculoskeletal in origin are caused by more serious pathologies or non-musculoskeletal sources. These pathologies may masquerade as musculoskeletal conditions in the early stages of the disease, presenting the clinician with a diagnostic challenge. Missed or delayed diagnosis of serious disease may have devastating consequences for patients. Early diagnosis and intervention are essential as this will lead to better outcomes. The clinician should always consider a broad range of differential diagnoses and aim to exclude serious pathology masquerading as a musculoskeletal condition, with the help of red flags.[28]

Red flags are potential warning signs that may indicate the presence of serious pathology.[26] Clinicians must be aware of potential red flags at all stages during every patient encounter, including face to face and telehealth appointments. In most situations, one new red flag on its own may not be enough to cause immediate concern, but it must be closely monitored. Multiple red flags, or in some cases where there is a significant medical history (e.g., past history of cancer) with concerning presenting features, one red flag, may be enough to consider further investigation depending on the context in which it is present.[20]

Some of the more common pathologies that mimic musculoskeletal conditions are presented in this chapter. It is essential that clinicians are aware of these, as early identification may lead to better outcomes.[20] All the pathologies discussed in this chapter may initially be "diagnosed" as variants of musculoskeletal shoulder pain. The presence of red flags, relevant risk factors and non-mechanical symptoms, should challenge the clinician's diagnosis, if the patient is not responding in the manner and timeline anticipated.

Malignancy

Primary bone and soft tissue tumors

Bone and soft tissue tumors are rare in incidence and account for less than 1% of all diagnosed malignancies.[22] In 2010, there were 531 new cases (around 10 per week) of primary bone tumors in the United Kingdom, in stark contrast to nearly 55,200 new cases of breast cancer reported every year. The rarity of these cases coupled with the heterogeneity in presentation pose a challenge to clinicians in diagnosis, because they commonly present to musculoskeletal services as mechanical conditions.[27] Cases of suspected tumors warrant management by specialists trained in musculoskeletal oncology to achieve optimal outcomes. Early referral is paramount since these tumors often grow rapidly, and outcome is directly related to the size at presentation. The upper extremity is the third most common site of occurrence of these tumors, with wide variation in their histological presentation.[11]

Symptoms and presentation

In the case of bone tumors, the commonest symptom is a constant, dull aching pain around the shoulder joint. Swelling and tenderness with persistent non-mechanical pain around the shoulder joint that increases at night warrants urgent evaluation to rule out a primary tumor.[21] A painful soft tissue mass that is greater than 5 cm (1.97 in), rapidly increasing in size, associated with non-mechanical pain, deep to the fascia, and with recurrence following excision, should be suspected as a tumor and requires urgent investigation and specialist referral.[21,74] Importantly, soft tissue tumors may not always be painful, with up to 71% of people with soft tissue sarcomas only seeking help when the lump increases in size.[21] Clinicians need to be aware that bone and soft tissue tumors have a bimodal age-specific incidence rate, with peaks in incidence seen in teenagers and young adults (around the second and third decades) and elderly patients.[21]

Malignant tumors commonly present with swelling around the shoulder that has been insidious in onset. Infiltration of soft tissues and muscles around the shoulder results in restricted shoulder movements usually associated with pain.[74] In elderly people, metastases to the shoulder are not uncommon and are usually associated with pain and loss of movement. Imaging is important to differentiate tumors from other causes of pain and loss of movement.[12]

Evaluation and investigations

Following clinical examination of the involved shoulder, imaging is important in the diagnosis of a malignant bone tumor involving the shoulder (Table 8.1).

CHAPTER EIGHT

Table 8.1 Summary of the most appropriate investigation for diagnosis and onward management

Modality	Primary tumors	Secondary tumors	Visceral	Rheumatology
Plain radiographs	A radiograph may establish the presence of visible moth-eaten periosteal reaction, characteristic of aggressive tumors.	A radiograph may show bone destruction which is typical of lung cancer, and bone sclerosis, which is typical of prostate cancer; destruction and sclerosis patterns are both common with breast cancer. A radiograph is used to establish risk of pathological fracture. [51]	Conventional radiography has limited diagnostic value in the assessment of most patients with abdominal pain.	Plain radiographs may show erosive change in primary inflammatory arthritides such as RA.
MRI	Used to evaluate the exact extent of the disease and assess the soft tissue involvement extension. STIR in addition to conventional T1 and T2 images help in evaluation of bone tumors and differentiation from infection and edema.[25]	MRI is used as the gold standard in detecting MBD. Where MBD is suspected, consider including the whole spine as MBD is more common in the axial skeleton.[68]	MRI is an emerging technique for the evaluation of abdominal pain that avoids ionizing radiation.[8]	May demonstrate synovitis (particularly if gadolinium contrast is used), effusion and erosion, as well as background rotator cuff pathology and degenerative change. However, in practice MRI is rarely used in the routine management of primary inflammatory arthritis, ultrasound being preferred.
CT	CT to evaluate the lesion involving the shoulder has a limited role, but can be used to define the size of the tumor and determine the presence of peripheral or satellite lesions.[53]	If there are contraindications for MRI, consider CT scan.	CT is the investigation of choice for general acute abdominal pain. CT is the most sensitive technique for depicting free intraperitoneal air and is valuable for determining the cause of any perforation.[67]	CT will demonstrate erosive and degenerative change; rarely used in practice by rheumatologists, more commonly used by orthopedic surgeons for perioperative planning.
Biopsy	Biopsy is mandatory for histological confirmation, operability assessment and therapy planning.[53] Usually a percutaneous needle biopsy under fluoroscopic guidance/ ultrasound guidance through the anterior fibers of the deltoid muscle is recommended.	Biopsy will help determine the primary cancer where there is suspicion of metastasis.		Synovial biopsy of the shoulder may demonstrate chronic inflammation in RA but is seldom used in practice unless co-existing pathology is suspected, such as infection.
Ultrasound			Ultrasonography is the initial imaging test of choice for patients presenting with right upper quadrant pain.	
Blood and urine tests	Blood tests reveal M proteins produced by myeloma cells and also another abnormal protein produced by myeloma cells – beta-2-mirogobulin. Urine samples reveal Bence Jones proteins characteristic of multiple myeloma.	There is no combination of inflammatory markers that can be used as a reliable rule-in or rule-out test strategy. The decision to test must be made in the context of other clinical findings.[75]		Raised inflammatory markers (ESR and CRP) are typical, but not universal in RA and PMR; rheumatoid factor is positive in approximately 85% of patients with RA; anti-CCP antibodies are predictive of erosive disease in RA.

Anti-CCP, anti-cyclic citrullinated peptides; CRP, C-reactive protein; CT, computerized tomography; ESR, erythrocyte sedimentation rate; MBD, metastatic bone disease; MRI, magnetic resonance imaging; PMR, polymyalgia rheumatica; RA, rheumatoid arthritis; STIR, Short TI Inversion Recovery.

Biopsy and histopathology analysis

"When tumor is the rumor, tissue is the issue": this adage remains relevant for suspected musculoskeletal tumors. For lesions in the shoulder, needle biopsy is recommended, followed by histopathological analysis to confirm diagnosis. Outcomes may be enhanced if the biopsy is performed by the treating surgeon, and histological analysis by an experienced pathologist.

Common malignant tumors of the shoulder and management

Multiple myeloma is a malignant tumor of bone marrow. It affects approximately 20 per million people each year. Most cases are seen in people aged 50–70 years old.[48] In the early stages there may be no symptoms or possibly vague symptoms such as fatigue and lethargy. Over time, bone pain, anemia and kidney dysfunction and general malaise ensue. It is an important differential in the work up of any suspected bone malignancy, and while it affects the entire skeleton, the shoulder is a common site. Blood investigations enable clinicians to reach the diagnosis, and with modern chemotherapy regimens, patients have better prognosis.[48]

Osteosarcoma is the second most common bone cancer. Annually it occurs in 2–3 per million people. Most cases occur in teenagers and young adults. Most osteosarcomas occur around the knee, followed by the hip, with the shoulder being the third most common site. Treatment involves neoadjuvant chemotherapy with the aim to shrink the tumor and decrease spread. Following chemotherapy, wide excision surgery is advised with at least a 2 cm (0.8 in) margin from the edges of the tumor.

Ewing's sarcoma most commonly occurs in people aged 5–20 years old. Radiotherapy and chemotherapy need be considered prior to or after surgery, depending on the disease progression in concurrence with the clinical oncology team. However, clinicians need to be mindful that prosthesis surgery in the upper extremity may be associated with challenges in functional outcomes, and complications including dislocation.[38]

Chondrosarcoma occurs most commonly in people aged 40–70 years old. Unlike osteosarcoma and Ewing's sarcoma, adjuvant therapy has a limited role in chondrosarcoma. Surgical resection of these tumors with adequate margins is the most appropriate management.

Myxofibrosarcoma is one of the most common soft tissue tumors that occurs mainly in people aged 50–70 years old, and is slightly more common in men than women. They are slow growing and painless,[72] and have a high rate of local recurrence and high risk of metastases.[16]

Liposarcoma accounts for up to 18% of all soft tissue sarcomas and can occur most commonly in the trunk, limbs, and abdomen. They are rare in people younger than 30 years old, and may present as a painful mass. These are low-grade neoplasms that rarely metastasize.[13]

Pancoast tumors represent 3–5% of all lung cancers, with a predilection to bony metastases.[15] The major risk factor is smoking, followed by older age, and they affect men more than women. These tumors develop in the apices of the lungs and infiltrate the thoracic inlet, which leads to a constellation of symptoms depending on which structures are invaded and compressed within this area. The tumor may invade muscles, upper ribs, thoracic vertebral bodies, subclavian vessels, the brachial plexus, and the thoracic autonomic chain, specifically the stellate ganglion.[53] Symptoms may include cough, hemoptysis, and dyspnea but are uncommon in the initial stages of the disease due to the tumor's location.[15] In the early stages the most reported symptom is shoulder pain due to the invasion of the pleura, upper ribs and brachial plexus. Symptoms may radiate down the arm in a typical ulnar nerve distribution, with physical signs relating to the invasion and compression of nervous, vascular, and bony structures within the thoracic inlet.[53]

- Tumors located in the anterior compartment of the thoracic inlet will affect the first intercostal nerve and upper ribs, subclavian and jugular veins, presenting with pain in the upper anterior chest wall and venous thrombosis.
- Tumors within the middle compartment will affect the brachial plexus, subclavian artery and phrenic nerves causing neurological symptoms of pain and paresthesia in the upper limb, potential paralysis of the diaphragm and arterial thrombosis.
- Tumors within the posterior compartment will affect the scalene muscles, subclavian and vertebral artery,

stellate ganglion, the sympathetic chain, long thoracic and accessory nerves, and vertebral bodies. Pain is reported within the axilla and medial aspect of the arm, and initial irritation of the sympathetic chain and specifically the stellate ganglion causes flushing and increased sweating ipsilaterally. Further invasion of the sympathetic chain may cause Horner's syndrome in 40% of cases,[43] which is associated with ipsilateral drooping of the eyelid, constricted pupil and lack of sweating (ptosis, miosis, and anhidrosis).[53]

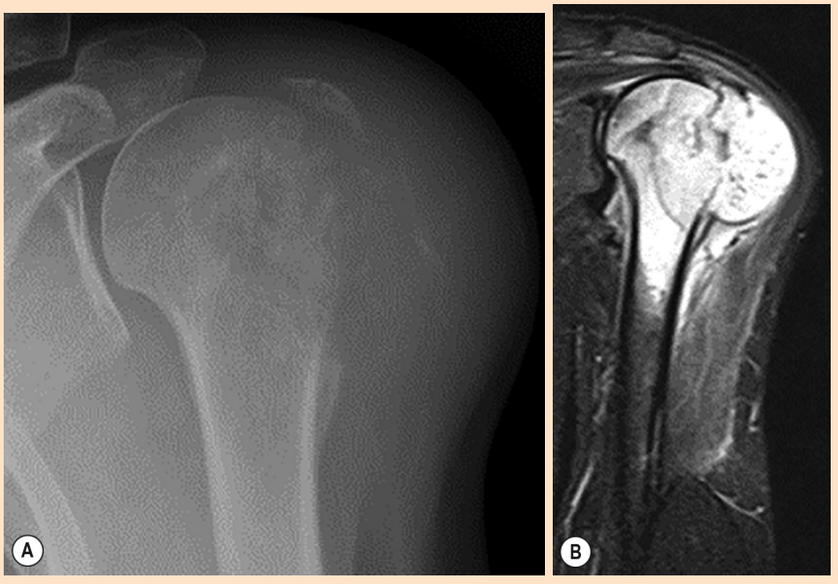
Management

All suspected malignant bone and soft tissue tumors of the shoulder require urgent onward referral and diagnostic work up (Table 8.1). Management and discussion in a sarcoma multidisciplinary team (MDT) ensures better coordination and communication to facilitate the most appropriate management.[53]

Box 8.1 Case study

A 22-year-old student presented to his general practitioner with a 3-month history of persistent pain, weight loss, and swelling in his left shoulder. There was no history of trauma. The swelling was approximately the size of a tennis ball. He did not have a fever, and on palpation no increased temperature was felt in the region of the swelling. Active and passive shoulder movements were limited.

An urgent plain radiograph of the left shoulder demonstrated a lesion in the humerus (Figure 8.1A), which prompted an urgent referral to a specialist unit. Further imaging (Figure 8.1B) confirmed an aggressive expansive lesion breaching the left proximal humeral cortex. Ultrasound-guided needle biopsy through the anterior deltoid muscle confirmed a high-grade osteosarcoma (Figure 8.1C) that was managed with neoadjuvant chemotherapy, followed by extra-articular wide excision surgery and prosthetic replacement (Figure 8.1D).



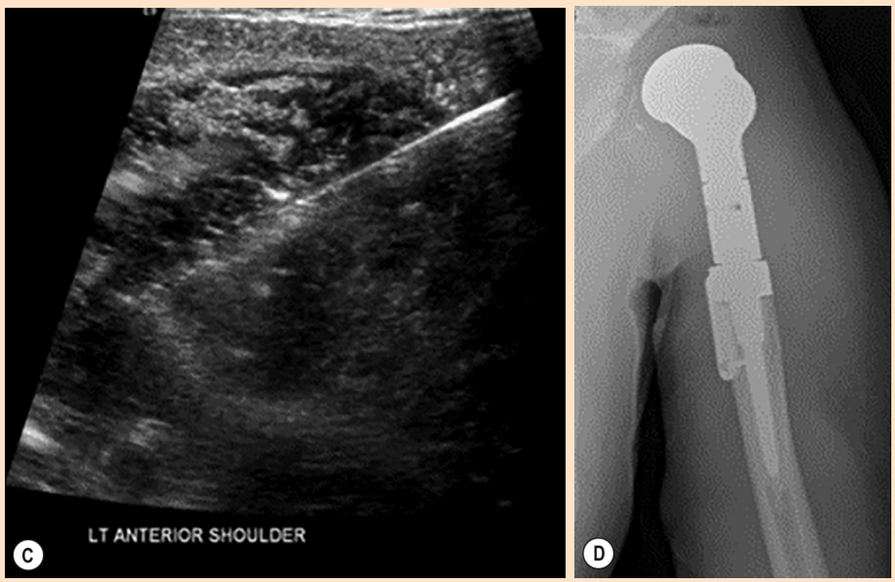


FIGURE 8.1
22-year-old student diagnosed with an osteosarcoma in the left humeral head. (A) Plain radiograph, (B) MRI, (C) ultrasound-guided needle biopsy, (D) wide resection and prosthetic replacement after neo-adjuvant chemotherapy.

Secondary cancers

Metastatic bone disease (MBD) tends to occur more commonly in the spine, but can affect the proximal long bones such as the humerus causing shoulder pain as the first presenting symptom.[51] The five most common cancers to metastasize to bone are of the breast, prostate, lung, kidney and thyroid.[12] MBD of the long bones occurs more commonly in people with breast and lung cancers.[39,55] A past history of cancer is a red flag and has a moderate diagnostic accuracy in relation to the development of MBD,[73] increasing the likelihood of serious pathology by 7% in primary care and 33% in emergency care.[34] A past history of cancer (particularly in cancers with a predilection to bone) should raise the clinician's index of suspicion of serious pathology, but on its own would not be sufficient to act on, as not all primary cancers go on to metastasize. Likewise, the absence of a history of cancer should not reassure the clinician of the lack of serious pathology, as MBD may be the first sign of an undiagnosed primary cancer.[29]

More effective medical treatment of primary cancers has led to longer life expectancies, but places survivors at greater risk of developing MBD.[5] MBD may occur as long as 10–20 years after a diagnosis of primary breast cancer. [45] MBD in the shoulder, particularly in relation to breast and lung cancers, may lead to a misdiagnosis of frozen shoulder, especially as frozen shoulder has a prolonged natural history.[60] Widespread MBD and visceral involvement are the consequences of untreated or late diagnosis and are associated with a poor prognosis.[69]

Clinical presentation

Pain arising from MBD is caused by a combination of ischemic, inflammatory, and neuropathic processes, and is

the consequence of destruction or compression of the bone and surrounding tissues.[17] Pain related to MBD may fluctuate, adding to the challenge of early identification, as individuals appear to respond to nonsurgical treatment.[29]

An intermittent localized ache is characteristic of bone pain and may be the first symptom. Pain may also be aggravated by movement.[36] Clearly these descriptors are also present in people with benign conditions.[19] However, in those individuals who have recurrent shoulder problems, an important question to ask is whether the type of pain they are experiencing is similar to previous episodes. In MBD, often the individual will report that this new onset of symptoms is different to the symptoms they have previously experienced, reporting a difference in the quality, location and type of pain.[20]

It is not until the late stages of MBD that pain becomes constant and unremitting, accompanied with significant night pain. Night pain is a common feature in musculoskeletal disorders, and a distinction needs to be made between night pain that is mechanical or caused by MBD. Where the individual describes being woken, with the need to get up and walk to ease the pain during the night, or that they are unable to sleep lying flat and routinely sleep upright in a chair, should raise concern.[19]

Physical examination

Objective findings may mimic rotator cuff pathology or frozen shoulder.[40,55] Tenderness in the greater tuberosity region of the humeral head may be a feature of a pathological fracture.[40] In the late stages, individuals may develop systemic features; a feeling of being unwell, fatigue, fever, or unexplained weight loss. Careful questioning possibly supported by investigations will help establish the relationship between symptoms and serious pathology.[20] If MBD is suspected, urgent referral for further investigation (Table 8.1) and specialist MDT management is essential.[12]

Visceral conditions

Visceral pain is extremely common and is experienced by more than 20% of the population.[31,77] The estimates of prevalence for dyspepsia, constipation and irritable bowel syndrome varies between conditions, and ranges between 1 in 10 to 1 in 2 people.[10,62] Almost all of the visceral organs have the potential to produce symptoms that masquerade as musculoskeletal pain in the thoracic spine, scapular, and shoulder region. Figure 8.2 illustrates the pain referral patterns of the visceral organs.

Visceral pain presentation

Visceral pain is most commonly described as a poorly defined, diffuse and vague,[9,24,61,62] although it may be experienced as sharp, stabbing, colicky pain.[56] Visceral pain generally starts in the midline and then radiates peripherally, and may produce somatic-type symptoms or symptoms in more distal areas.[23,24] A full and thorough clinical examination is required to eliminate the viscera as a potential source of shoulder pain.

Clinical examination

Identifying viscerally referred shoulder pain is a clinical challenge, but clinicians should always consider it as a possible source of the patient's symptoms. Clinicians should ask patients about visceral function, particularly about organs that may refer to the shoulder. This should include a past or current history of cardiac, respiratory, and gastrointestinal symptoms, investigations or concerns, with a clear explanation of the purpose of the questions.

Liver

The liver is the largest organ, responsible for a wide range of tasks, including toxin breakdown, fighting infection, and metabolism of nutrients. Symptoms commonly occur in the later stages of liver disease,[79] and may be experienced as local, right lower thoracic, and right shoulder pain.[54] People with a history of high alcohol intake, obesity, hepatitis, hemochromatosis, or primary biliary cirrhosis may be more likely to develop shoulder symptoms referred from their liver.[2] Clinicians should also be watchful for and question the patient about jaundice, a pruritic rash, yellowing of the eyes, dark circles around the eyes, sweating, fever, strong body odor, bad breath, pale or gray stools, dark urine, fatigue, weight loss, nausea and vomiting, bloating, and testicular swelling.

Gall bladder

Gallstones affect between 5–25% of the population and are more common in women, people who are obese,

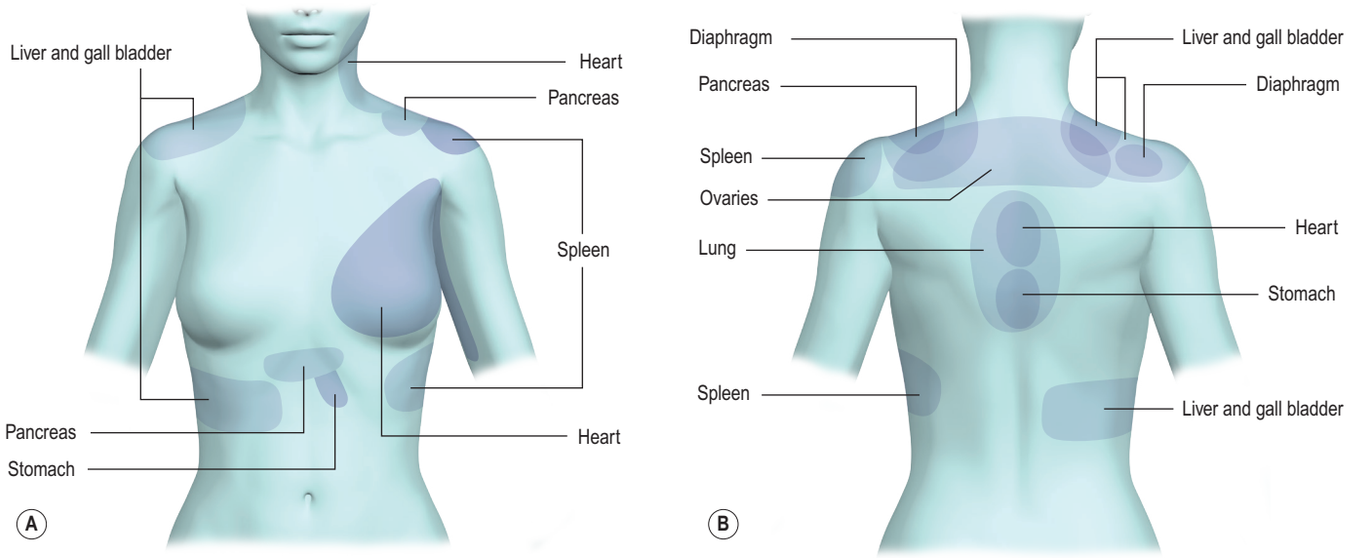


FIGURE 8.2
(A) Anterior and (B) posterior pain referral patterns of visceral organs.
(Based on original drawings by Mr Allan Mercer.)

and older age groups.[32] The gall bladder is positioned below the liver and pain referral occurs in a similar pattern to the liver. Symptoms are commonly caused by calculous cholecystitis (95% of cases), where the cystic duct between the liver and gall bladder becomes blocked and inflamed due to a build-up of biliary sludge/stones.[49] The gall bladder stores bile to help with digestion, so symptoms usually relate to ingestion of fatty, spicy, processed, and high carbohydrate foods. People may initially experience colic-type symptoms, giving severe pain for up to half an hour that then recedes, and may progress to a constant ache.

Pancreas

Pancreatitis is associated with diabetes, high alcohol intake, obesity, and gallstones, though often the cause is unclear. Pancreatic cancer is often hard to detect until the latter stages of the disease and may be associated with general fatigue, weight loss, fever, jaundice, and changes to stools (lighter in color) and urine (darker in color). Pain is predominantly experienced in the epigastric region; the pancreas can also refer to the mid thoracic spine, and there are also documented cases of metastatic disease from the pancreas causing cervical and left or right shoulder pain.[1,46]

Heart

Chest pain and shortness of breath are common symptoms of cardiac disease. Referred pain in the neck, thorax, jaw, throat, and left shoulder and arm may be experienced. Typically, symptoms are activity-related but may occur because of unhealthy stress. Paresthesia, dizziness, nausea and anxiety, or a sense of impending doom are other cardiac-related symptoms.

Lung/pleura

Depending on the area and nature of the pathology, the lungs and pleura may refer to the thorax, or to either shoulder.[44,57,76] Referred pain may be associated with dyspnea, cough or hemoptysis. A smoking history and detailed medical history of any lung disease should be elicited.

Stomach

Stomach pathology most commonly refers to the epigastric region or causes dysphagia; it may refer to the mid to upper thoracic spine and left shoulder. Associated symptoms may include flatus, belching, a feeling of fullness and abdominal bloating, nausea, heartburn, vomiting, reflux, weight loss, and anorexia.

Spleen

The spleen is in the left upper quadrant next to the stomach and is an important part of the immune system. It may be damaged by abscess or traumatic injury.[66,71] Liver disease, anemia, and blood cancers such as lymphoma and leukemia may also be associated with symptoms.[78] If enlarged or infected, the spleen may cause irritation of the diaphragm, and refer pain to the left shoulder via the phrenic nerve (C3, C4, C5).[18] Associated symptoms may be bruising easily and fatigue.

Ovaries

Although unusual, the ovaries may refer pain to the shoulders. Large ovarian cysts may cause pressure on the diaphragm, or ruptured cysts and blood within the peritoneum can also cause irritation of the diaphragm and referral to the shoulder via the phrenic nerve.[50] Shoulder pain will be non-mechanical and may be associated with abdominal pain, nausea and vomiting, and changes to menses.

Physical examination

If there are any suspicions of visceral causes for shoulder symptoms then abdominal inspection, palpation, and auscultation should be performed. If this is not within your scope of practice, appropriate referral is required.

The abdomen should be inspected for: asymmetry, or any obvious lumps and bumps; any signs of injury; bruising (Grey Turner sign that may indicate internal bleeding); skin changes such as spider nevi (present in liver disease); and pulsatile masses that may indicate abdominal aortic aneurysm. Palpation should be performed in a structured and methodical way. The aim is to determine whether there are any painful areas, and whether there are any firm and palpable/pulsatile masses within the abdomen. It may also be possible to reproduce the patient's symptoms with palpation, so it is important to monitor their specific symptoms throughout the process.

Inflammatory conditions

Although soft tissue and degenerative pathology are considerably more common, when presented with a patient with shoulder symptoms the clinician should consider whether this presentation might be the first manifestation of a systemic inflammatory rheumatic disease, such as polymyalgia rheumatica (PMR) or rheumatoid arthritis (RA). These form a heterogeneous group of immune-mediated disorders of unknown etiology that usually require systemic immunomodulatory therapies.

Polymyalgia rheumatica

PMR should be the first inflammatory rheumatic condition to consider when assessing a person with shoulder pain. PMR is a common clinical syndrome of unknown etiology seen in people over the age of 50, characterized by pain and stiffness in the neck, shoulders, pelvic girdle and hips. Symptoms are usually symmetrical but may be assymetrical. The stiffness is particularly severe after rest and may prevent the patient getting out of bed. The onset can be abrupt or more insidious and, along with the related condition giant cell arteritis, may present with a low-grade fever. These conditions therefore both need to be considered in the investigation of a pyrexia of unknown origin. In addition to fever, people with PMR may be systemically unwell, experiencing general malaise, fatigue and weight loss.[14]

As with PMR, the prevalence of rotator cuff related shoulder pain (RCRSP) and symptomatic osteoarthritis (OA) in the glenohumeral and/or acromioclavicular joints also increases with age. This may complicate the clinical picture, and diagnoses of RCRSP and OA based on imaging alone must be avoided. The primary underlying pathology in PMR is a synovitis and subacromial bursitis. Shoulder stiffness in PMR usually affects all directions of movement and needs to be considered with other causes of shoulder stiffness. There is usually minimal tenderness or weakness in PMR, and swelling is rare.

Typically, PMR causes a fairly marked acute phase response, with elevation of the inflammatory markers

erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), which are also used to help guide the response to treatment. Very occasionally inflammatory markers are normal, creating a diagnostic challenge for the clinician. A quick and dramatic response to low doses (15 mg/day) of corticosteroids is a classic feature of PMR. It is not uncommon to require corticosteroids for several years, and to avoid relapse, the dose must be tapered gradually.[65]

Rheumatoid arthritis

Rheumatoid arthritis (RA) is the most common autoimmune chronic inflammatory rheumatic disease, with a population prevalence of 0.5–1%,[63] and is more common in women of childbearing age. The shoulder is involved in 50–60% of cases of RA and, like PMR, symptoms tend to be symmetrical. However, patients are more likely to present with symptoms in other regions first, and RA most commonly presents as a symmetrical polyarthritis affecting the small joints of the hands and feet. The onset may be acute, but is more often subacute or insidious, the latter usually resulting in a poorer prognosis as it is more difficult to control with immunosuppressive drugs. There is also a greater risk of developing erosive joint damage.[33] Patients presenting with an early inflammatory polyarthritis, in whom a firm diagnosis is yet to be established, are more likely to eventually be diagnosed with RA if they have shoulder involvement.[6]

Rheumatologists often observe a history of previous soft tissue disorders, including adhesive capsulitis and rotator cuff tendonitis in patients with newly diagnosed RA. The possibility that a patient may be developing the latter or another systemic inflammatory arthritis should always be considered in patients who appear to have multiple soft lesions of increasing frequency. Indeed, tenosynovitis appears as a common early finding in patients with RA, particularly in those patients who have anti-cyclic citrullinated peptide (anti-CCP) antibodies.[41] In the elderly, a PMR-like presentation of RA is well recognized.

Classic deformities are observed in the hands in people diagnosed with RA, but deformity is rare in the shoulder except in severe or suboptimally treated disease. If the disease remains active with uncontrolled inflammation, irreversible damage, deformity, and instability may occur.[70] Synovitis in the shoulder may lead to effusions, which can extend into the subacromial and subdeltoid spaces, particularly in the presence of rotator cuff damage. As in the hands, secondary muscle wasting is observed. Persistent rheumatoid effusions usually contain thick, inspissated inflammatory fluid, sometimes containing cholesterol crystals in addition to neutrophils, monocytes and synoviocytes. The fluid may become loculated, and therefore difficult to aspirate, and fistulae may form.[4]

In the person with RA involving the shoulder, a loss of external rotation is a common sign although more typically a global restriction of movement is observed, similar to that seen in PMR, particularly with more advance disease.[52] Anterior upper arm pain and tenderness in the bicipital groove is common and may indicate bicipital tendon involvement. There is a risk of bicipital tendon rupture if persistent inflammation is left unchecked.[64]

The management of RA requires a multidisciplinary team, using both pharmacological and non-pharmacological approaches. Suppression of the underlying inflammatory disease using anti-inflammatory and immunosuppressive drug therapy is required.[65] Specific to the shoulder, in addition to arthrocentesis for larger effusions, corticosteroid injections to the glenohumeral joint and subacromial bursa are used to control symptoms. Intramuscular corticosteroid injections are also used, especially during an acute flare of symptoms. These are frequently administered into the deltoid muscle which increases the possibility of subcutaneous fat atrophy. Osteonecrosis of the humeral head may occur in RA or develop secondary to systemic corticosteroid therapy.[47]

Other primary inflammatory arthropathies

Shoulder symptoms are associated in the seronegative inflammatory arthritis group of diseases, although are less common than in RA.[58] Asymmetrical disease is more likely in people with seronegative arthropathies. For example, the disease is asymmetric in approximately 50% of those diagnosed with psoriatic arthritis. Enthesitis tends to be the predominant underlying pathology in this group of diseases, rather than synovitis.[37] Additional involvement of the sternoclavicular joint often points to one of the seronegative arthropathies rather than RA. Synovitis in the sternoclavicular joint causes localized swelling and tenderness, with pain in the joint on arm elevation. Severe symptoms in a less commonly affected joint such as this should raise the

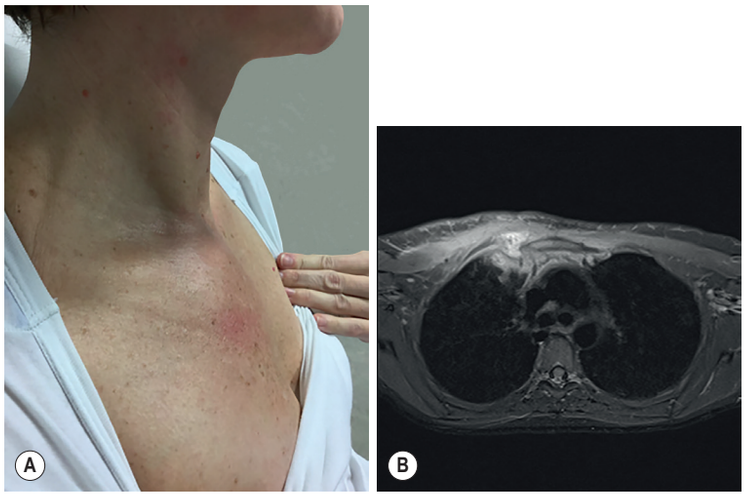


FIGURE 8.3
(A) Infection due to *Staphylococcus aureus* in the right sternoclavicular joint in a 40-year-old woman with psoriatic arthritis treated with sulfasalazine and the TNF-inhibitor adalimumab. (B) Axial MRI at the level of the sternoclavicular joints showing increased signal on T2-weighted images due to soft tissue swelling, bone edema and expansion.

index of suspicion for more serious complications such as infection (Figure 8.3). As in RA, there is a risk of rupture of the long head of biceps in psoriatic arthritis.[7]

Crystal arthropathies

Gout is the most common inflammatory arthritis affecting middle-aged men, and is caused by the deposition of monosodium urate crystals in the joint. This leads to an intense inflammatory response. It most commonly affects lower limb joints, particularly the first metatarsophalangeal joint (podagra); involvement of the shoulder is extremely unusual. However, shoulder involvement in pseudogout (calcium pyrophosphate deposition disease (CPPD)) is common.[59] This is another common form of inflammatory arthritis in the elderly, usually presenting with abrupt-onset severe pain and restricted movement, often accompanied by marked tenderness and erythema. Desquamation over the joint as the acute arthritis settles is a clue to the diagnosis. Chondrocalcinosis is usually seen on radiographs of the affected joint. As with gout, treatment of the acute attack involves NSAIDs, colchicine and corticosteroids (both orally and by injection).

Lupus, inflammatory myositis, and other autoimmune connective tissue disorders

Arthralgia is a very common symptom in systemic lupus erythematosus (SLE), but joint swelling due to synovitis is much less pronounced compared to RA. The inflammatory arthritis seen in SLE is non-erosive. When erosions are found on imaging, this suggests the presence of overlapping RA (formerly termed "rhupus"). Although synovitis in smaller joints is more common, the shoulder may be involved in SLE, as it may in all other multisystem autoimmune connective tissue disorders, such as Sjögren's syndrome and scleroderma (systemic sclerosis). In the latter, dermal fibrosis leads to skin thickening. Although rare, this can affect the shoulder girdle area, with consequent restriction of movement. Subcutaneous and periarticular calcinosis around the shoulder is also described. Fibrosis of ligaments and the joint capsule also contributes to restriction of movement in scleroderma, and fibrosis in the synovium is also observed. Compared to that seen in RA, the synovitis seen in SLE and scleroderma is generally less intense, and erosion is less common.[3]

The primary inflammatory muscle diseases polymyositis and dermatomyositis may present with shoulder pain and stiffness mimicking PMR, but unlike the latter, weakness is a far more pronounced symptom and sign. A proximal myopathy will unusually be apparent on clinical examination, with additional (and usually more severe) lower limb involvement. Dermatomyositis causes typical skin changes such as a heliotrope rash around the eyes, a "shawl" rash on the upper chest, and Gottron's papules on the hands.

Blood tests in patients with polymyositis and dermatomyositis will usually show elevated levels of muscle enzymes such as creatine kinase. Dermatomyositis can be a paraneoplastic phenomenon; testing for myositis-specific antibodies can assist in assessing the patient's risk of

an associated malignancy. As in other inflammatory rheumatic conditions such as RA and PMR, corticosteroids are essential in the management of inflammatory myopathies, but additional immunosuppressive drugs are invariably also used for their steroid-sparing and immunomodulatory effects. Patients with autoimmune connective tissue disorders such as SLE, scleroderma, and primary inflammatory myositis have an increased risk of requiring rotator cuff surgery compared to age- and sex-matched controls.[35]

Involvement of the shoulder is also seen in people with the multisystem chronic granulomatous disease sarcoidosis, although is rare relative to other regions such as the ankle and hands.[42] A chronic destructive arthropathy may develop, and synovial biopsy may reveal the presence of typical non-caseating granulomas, although more typically shows nonspecific inflammatory change.

Shoulder pain may be experienced in people with the small vessel vasculitides associated with anti-neutrophil cytoplasmic antibodies (ANCA), such as granulomatosis with polyangiitis, but a true inflammatory arthritis in these diseases is rare.

Conclusion

While most people presenting with shoulder and thoracic pain will not have a serious pathology, the clinician should always consider a range of differential diagnoses as a potential source of symptoms, especially if symptoms are atypical or not responding to treatment. Knowledge of these conditions and their presentation will ensure timely investigation and management and overall better outcomes. In summary, "Things are not always what they seem – be informed and awake."[30]

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