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Persistent Shoulder Pain Revealing a Metastatic Proximal Humeral Lesion from Occult Lung Adenocarcinoma: An Interdisciplinary Diagnostic Challenge

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ABSTRACT

Shoulder pain is a common complaint encountered in primary care and is most frequently attributed to benign musculoskeletal conditions. However, persistent symptoms that fail to respond to conventional treatment may occasionally represent the first manifestation of a serious underlying disease. Bone metastases are a common complication of advanced lung cancer, yet they rarely present as the initial clinical feature in the absence of respiratory symptoms. We report the case of a 58-year-old man who presented with progressive atraumatic shoulder pain initially diagnosed as rotator cuff tendinopathy in a family medicine setting. Despite conservative management, his symptoms worsened and became associated with nocturnal pain, fatigue, and unintentional weight loss. Further investigation revealed anemia, elevated inflammatory markers, and an osteolytic lesion of the proximal humerus. Advanced imaging identified a previously undiagnosed pulmonary mass, and histopathological examination confirmed metastatic lung adenocarcinoma. The patient underwent prophylactic orthopaedic fixation of the humerus followed by systemic oncological treatment. This case highlights the importance of recognizing red-flag symptoms in patients with persistent musculoskeletal pain and emphasizes the value of interdisciplinary collaboration between family medicine, internal medicine, radiology, pathology, orthopaedic oncology, pulmonology, and medical oncology.

Keywords

Shoulder Pain, Bone Metastasis, Lung Adenocarcinoma, Proximal Humerus, Primary Care, Orthopaedic Oncology, Diagnostic Challenge.

Introduction

Shoulder pain is among the most frequent musculoskeletal complaints encountered in primary care practice, accounting for a substantial proportion of outpatient consultations worldwide. The majority of cases are related to benign conditions such as rotator cuff tendinopathy, adhesive capsulitis, acromioclavicular joint disease, and subacromial impingement syndrome. Consequently, initial management often involves conservative measures including analgesia, physiotherapy, and activity modification.

Although uncommon, malignant disease should remain within the differential diagnosis of persistent musculoskeletal pain, particularly when symptoms fail to respond to standard treatment or are accompanied by systemic features. Metastatic bone disease represents the most common malignant process affecting the skeleton and frequently arises from primary cancers of the lung, breast, prostate, thyroid, and kidney [1,2].

Lung cancer remains the leading cause of cancer-related mortality worldwide [3,4]. Most patients present with respiratory symptoms such as cough, dyspnoea, chest pain, or haemoptysis. However, a minority of patients initially present with extrapulmonary manifestations, creating diagnostic difficulties and potentially delaying treatment. In rare instances, bone metastases may represent the first clinical manifestation of an otherwise occult

primary lung malignancy [5,6].

We report a case of persistent shoulder pain initially managed as a benign musculoskeletal disorder that ultimately led to the diagnosis of metastatic lung adenocarcinoma. This case illustrates the importance of clinical vigilance, repeated assessment, and multidisciplinary collaboration when evaluating patients with persistent musculoskeletal symptoms.

Case Presentation

A 58-year-old man presented to a family medicine clinic with a six-week history of progressive left shoulder pain. The pain developed gradually without preceding trauma and was initially localized to the lateral aspect of the shoulder. He described a dull, aching discomfort that progressively intensified and began interfering with daily activities, including dressing, lifting objects, and sleeping on the affected side.

The patient denied fever, chills, cough, dyspnea, hemoptysis, chest pain, or recent infections. His medical history included hypertension controlled with ramipril. He was a former smoker with an estimated 30-pack-year smoking history and had quit smoking approximately five years before presentation. There was no personal history of malignancy and no significant family history of cancer.

Physical examination demonstrated mild tenderness over the proximal humerus and discomfort during active shoulder abduction beyond 90 degrees. Passive range of motion was largely preserved, although terminal abduction and external rotation elicited pain. There was no visible swelling, erythema, or deformity. Neurological examination was normal, and distal pulses were intact.

Given the absence of trauma and the apparent mechanical nature of the symptoms, an initial diagnosis of rotator cuff tendinopathy was considered. Conservative management was initiated, including nonsteroidal anti-inflammatory drugs, activity modification, and referral for physiotherapy.

Three weeks later, the patient returned for reassessment because of worsening symptoms. He reported increasing pain severity despite strict adherence to treatment recommendations. The pain had become more pronounced during the night, frequently waking him from sleep. He also reported progressive fatigue and an unintended weight loss of approximately five kilograms over the preceding two months. These developments prompted reconsideration of the initial diagnosis.

Given the progression of symptoms and the emergence of constitutional features, laboratory investigations were performed to evaluate for systemic disease. Results demonstrated normocytic anaemia (haemoglobin 10.8 g/dL), elevated inflammatory markers (ESR 72 mm/h, CRP 38 mg/L), and mild hypercalcaemia (corrected serum calcium 10.9 mg/dL), raising suspicion for an underlying malignant process (Table 1). Renal and liver function tests were within normal limits.

Table 1: Key Laboratory Findings at Reassessment.

Parameter	Result	Reference range
Hemoglobin	10.8 g/dL	13.5-17.5 g/dL
ESR	72 mm/h	<20 mm/h
CRP	38 mg/L	<5 mg/L
Corrected Serum Calcium	10.9 mg/dl	8.5-10.5 mg/dL
Alkaline Phosphatase	168 U/L	40-130 U/L

Plain radiographs of the left shoulder demonstrated an ill-defined osteolytic lesion involving the proximal humeral metaphysis associated with cortical thinning and loss of normal trabecular architecture (Figure 1A). These findings raised concern for an underlying malignant process. Magnetic resonance imaging of the shoulder subsequently revealed an aggressive intramedullary lesion occupying the proximal humerus with cortical destruction and extension into adjacent soft tissues (Figure 1B). The radiological appearance was highly suggestive of metastatic disease.

The patient was subsequently referred to internal medicine and orthopaedic oncology services for further evaluation. Contrast-enhanced computed tomography of the chest, abdomen, and pelvis identified a 3.8-cm spiculated mass in the right upper lobe of the lung accompanied by mediastinal lymphadenopathy (Figure 1C). No alternative primary malignancy was identified. Collectively, the imaging findings raised strong suspicion for a primary pulmonary malignancy with secondary skeletal involvement.

A CT-guided core needle biopsy of the humeral lesion was performed. Histopathological examination demonstrated moderately differentiated adenocarcinoma composed of malignant gland-forming epithelial cells with moderate nuclear atypia and focal necrosis (Figure 1D). Immunohistochemical analysis revealed strong nuclear positivity for thyroid transcription factor-1 (TTF-1) (Figure 1E) and positivity for cytokeratin 7 (CK7), while cytokeratin 20 (CK20) was negative. The immunophenotypic profile strongly supported pulmonary adenocarcinoma as the primary source.

Orthopaedic assessment revealed substantial cortical destruction of the proximal humerus and a high risk of impending pathological fracture. Based on lesion location, osteolytic appearance, lesion size exceeding two-thirds of the cortical diameter, and severe functional pain, the patient's Mirels score was estimated at 10, indicating a high risk of pathological fracture and supporting prophylactic surgical stabilisation. Following multidisciplinary discussion, prophylactic intramedullary fixation was performed to stabilise the bone and preserve upper limb function. Postoperative radiographs confirmed satisfactory implant positioning and stabilisation of the proximal humerus (Figure 1F). The postoperative course was uncomplicated.

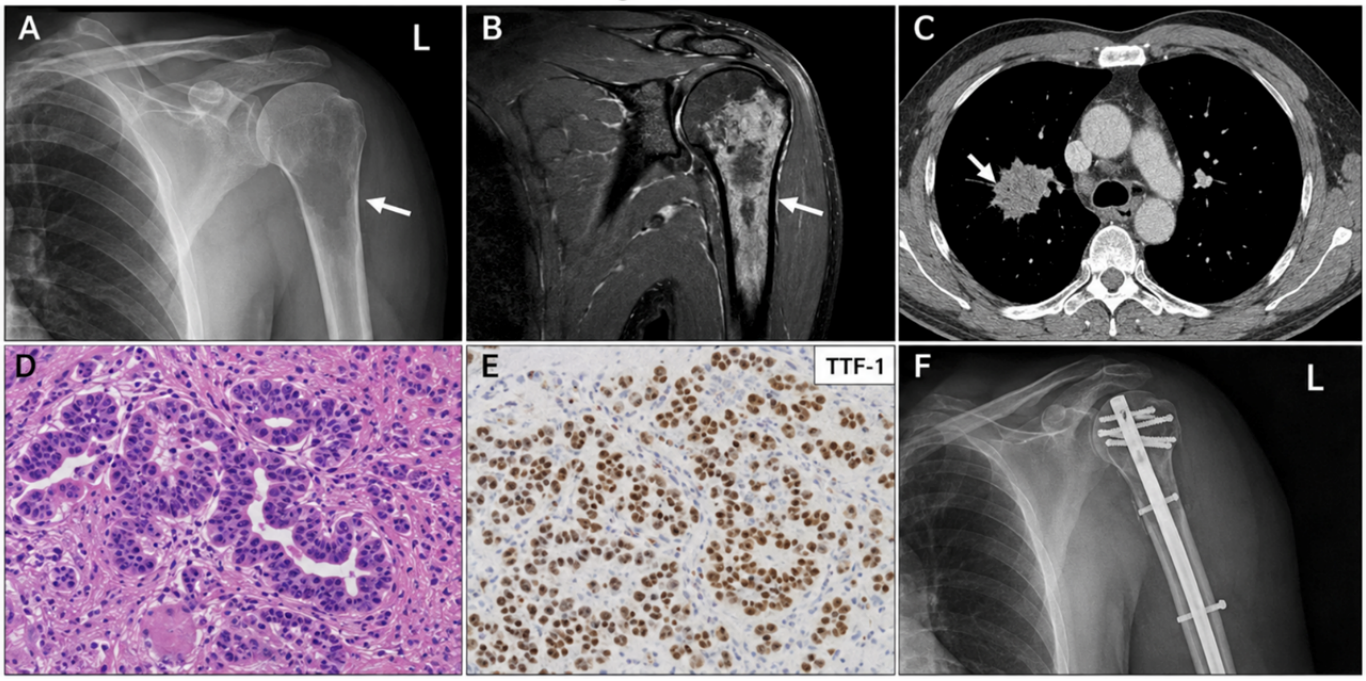


Figure 1: Imaging and histopathological findings in a patient with a metastatic proximal humeral lesion secondary to lung adenocarcinoma. (A) Plain radiograph of the left shoulder demonstrating an ill-defined osteolytic lesion involving the proximal humeral metaphysis with cortical thinning (arrow). (B) Coronal T2-weighted magnetic resonance image showing an aggressive intramedullary lesion with cortical destruction and soft tissue extension (arrow). (C) Contrast-enhanced computed tomography of the chest revealing a spiculated right upper lobe pulmonary mass (arrow) associated with mediastinal lymphadenopathy. (D) Histopathological examination (hematoxylin and eosin stain, ×200) demonstrating malignant gland-forming epithelial cells consistent with adenocarcinoma. (E) Immunohistochemical staining showing strong nuclear positivity for thyroid transcription factor-1 (TTF-1), supporting pulmonary origin (×200). (F) Postoperative radiograph following prophylactic intramedullary fixation of the left humerus.

Positron emission tomography-computed tomography demonstrated intense fluorodeoxyglucose (FDG) uptake within the right upper lobe pulmonary mass, mediastinal lymph nodes, proximal humeral lesion, and multiple thoracic vertebral bodies, consistent with metastatic disease. The patient was subsequently referred to medical oncology and commenced systemic treatment according to current guidelines for advanced lung adenocarcinoma.

At six-month follow-up, the patient reported significant improvement in pain control and maintained satisfactory upper limb function. He remained under regular oncologic surveillance while continuing systemic therapy.

Discussion

Atypical Presentation of Occult Lung Cancer

Lung cancer remains one of the leading causes of cancer-related mortality worldwide and is frequently diagnosed at an advanced stage [3,4]. The majority of patients present with respiratory symptoms such as persistent cough, dyspnea, chest pain, hemoptysis, or recurrent respiratory infections. However, a subset of patients initially present with extrapulmonary manifestations resulting from metastatic disease, paraneoplastic syndromes, or systemic effects of malignancy. Such presentations can significantly delay diagnosis because clinical attention is often directed toward the symptomatic organ system rather than the underlying primary malignancy.

The present case illustrates an uncommon scenario in which metastatic bone disease was the first clinically apparent manifestation of an occult lung adenocarcinoma. Notably, the patient denied cough, shortness of breath, chest pain, or constitutional symptoms during his initial presentation. Consequently, the clinical picture appeared consistent with a common musculoskeletal disorder. This diagnostic challenge is particularly relevant in primary care, where shoulder pain is among the most frequent reasons for consultation and is overwhelmingly caused by benign conditions.

Several studies have demonstrated that bone metastases may occasionally represent the first indication of an underlying malignancy [2,5]. Lung cancer possesses a particularly strong tendency for skeletal dissemination because of its rich vascular network and early haematogenous spread [5,6]. The spine, ribs, pelvis, femur, and humerus are among the most frequently involved skeletal sites [1,5].

The absence of respiratory symptoms in the present case highlights the importance of maintaining a broad differential diagnosis when evaluating persistent musculoskeletal pain, especially when the clinical course deviates from expectations. While uncommon diagnoses should not dominate initial decision-making, clinicians should remain alert to features that suggest a more serious underlying process.

Diagnostic Challenges in Family Medicine and Primary Care

From a family medicine perspective, this case underscores the importance of longitudinal assessment and diagnostic reassessment. At initial presentation, the patient's symptoms were entirely compatible with rotator cuff tendinopathy, one of the most common causes of shoulder pain. Conservative treatment was therefore reasonable and consistent with established clinical practice.

One of the defining strengths of primary care is the opportunity for follow-up evaluation. Reassessment provides clinicians with the ability to observe symptom progression, monitor response to treatment, and identify emerging red flags. In this patient, failure to improve despite appropriate management represented the first indication that the original diagnosis might be incomplete or incorrect.

Several warning signs subsequently emerged, including progressive pain severity, nocturnal pain, fatigue, and unintentional weight loss. Collectively, these findings increased the likelihood of serious pathology and justified further investigation. Night pain is particularly important because it is frequently associated with malignant, infectious, or inflammatory processes rather than simple mechanical disorders.

This case demonstrates how diagnostic accuracy often depends not solely on the initial consultation but on the clinician's willingness to reconsider previous assumptions when new information becomes available. Anchoring bias, in which clinicians become excessively attached to an initial diagnosis, may contribute to delayed recognition of malignancy in patients presenting with common symptoms. Continuous diagnostic vigilance is therefore essential in primary care settings.

Internal Medicine Perspective: The Significance of Systemic Findings

The laboratory abnormalities identified during further evaluation provided critical clues regarding the presence of an underlying systemic disease. Normocytic anemia, elevated inflammatory markers, and hypercalcemia collectively suggested a pathological process extending beyond the musculoskeletal system.

Anaemia is frequently encountered in patients with advanced malignancy and may arise through multiple mechanisms, including chronic inflammation, bone marrow infiltration, nutritional deficiencies, or occult blood loss [1].

Hypercalcaemia deserves particular attention because it represents one of the most common metabolic complications of malignancy [6]. In lung cancer, hypercalcaemia may develop through local osteolytic destruction caused by bone metastases or through secretion of parathyroid hormone-related peptide by tumour cells [6].

From an internal medicine standpoint, the integration of clinical findings with laboratory abnormalities was essential in broadening the diagnostic evaluation beyond a localized orthopedic disorder. This interdisciplinary approach facilitated timely diagnosis and expedited referral to appropriate specialist services.

Imaging and Histopathological Diagnosis

Imaging played a pivotal role in establishing the diagnosis. Plain radiography remains an important first-line investigation for persistent bone pain because it can reveal structural abnormalities that may not be apparent on physical examination alone. In this case, radiographs demonstrated an osteolytic lesion involving the proximal humerus, immediately raising suspicion for an aggressive pathological process.

Magnetic resonance imaging provided further characterization of the lesion and demonstrated features highly suggestive of malignancy, including cortical destruction and soft tissue extension. MRI offers excellent sensitivity for detecting marrow infiltration and is particularly valuable when evaluating suspected metastatic disease [6].

Once a malignant lesion is identified, histopathological confirmation remains mandatory before definitive treatment planning. The immunohistochemical profile observed in this patient, characterized by positivity for TTF-1 and CK7 and negativity for CK20, strongly supported pulmonary adenocarcinoma as the primary source of metastatic disease. Tissue diagnosis not only establishes the origin of the malignancy but also guides therapeutic decision-making and prognostic assessment.

Orthopaedic Oncology Perspective and Prevention of Pathological Fracture

The orthopaedic implications of metastatic bone disease are substantial. Skeletal metastases can result in severe pain, reduced mobility, and pathological fractures, all of which significantly impair quality of life [1]. The proximal humerus represents one of the most common locations for appendicular skeletal metastases because of its abundant blood supply and active marrow content [1].

The extensive cortical destruction visible on radiography and MRI in the present case (Figure 1A–B) substantially increased the risk of pathological fracture and supported the decision to proceed with prophylactic surgical stabilisation. Prophylactic stabilisation was considered preferable to waiting for fracture occurrence. Multiple studies have demonstrated that prophylactic fixation of impending pathological fractures is associated with reduced surgical morbidity, shorter hospitalisation, improved postoperative function, and superior pain control compared with fixation performed after fracture development [1,7].

Assessment tools such as the Mirels scoring system may assist clinicians in estimating fracture risk by evaluating lesion size, anatomical location, radiographic appearance, and pain severity [7].

The successful stabilisation of the humerus in this patient preserved upper limb function and facilitated subsequent oncological treatment, illustrating the important role of orthopaedic oncology within multidisciplinary cancer care.

Multidisciplinary Management and Clinical Implications

Perhaps the most important lesson from this case is the value of interdisciplinary collaboration. The diagnostic pathway involved multiple specialties, each contributing unique expertise to patient care. Family medicine provided initial assessment and longitudinal follow-up. Internal medicine recognized systemic abnormalities and coordinated further investigation. Radiology identified the metastatic lesion and occult pulmonary mass. Pathology established the definitive diagnosis through tissue analysis. Orthopaedic oncology prevented pathological fracture through surgical stabilization. Medical oncology subsequently initiated systemic treatment directed at the primary malignancy.

The integration of these disciplines enabled timely diagnosis and management despite an initially misleading presentation. Such collaboration is increasingly important as cancer care becomes more complex and specialized.

For clinicians practicing in primary care, this case reinforces several key principles. Persistent musculoskeletal pain should not automatically be attributed to benign pathology, particularly when symptoms fail to improve with appropriate treatment. Constitutional symptoms, nocturnal pain, unexplained laboratory abnormalities, and progressive functional impairment should prompt further evaluation. Early recognition of these warning signs may facilitate diagnosis before catastrophic complications such as pathological fracture occur.

Conclusions

Persistent shoulder pain may rarely represent the first manifestation of occult malignancy. This case demonstrates how metastatic lung adenocarcinoma can initially present as an isolated musculoskeletal complaint in the absence of respiratory symptoms. Recognition of red-flag features, timely diagnostic reassessment, and multidisciplinary collaboration were critical in establishing the diagnosis and preventing pathological fracture. Clinicians should maintain a high index of suspicion when common musculoskeletal complaints follow an atypical clinical course or fail to respond to standard treatment.

Limitations

This report describes a single clinical case, limiting the generalizability of the findings. In addition, follow-up was limited to six months, preventing assessment of long-term oncologic outcomes, disease progression, implant durability, and overall survival. Further studies are required to better characterize atypical musculoskeletal presentations of metastatic lung cancer in primary care settings.

Patient Consent and Ethics Statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Ethical approval was not required according to institutional guidelines for single case reports.

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