Subscapularis Myotendinous Junction Tears Presenting with Posterior Shoulder Pain in Overhead Throwing Athletes

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Introduction

Shoulder pain is common in overhead throwing athletes due to the extreme stresses placed on the shoulder during the throwing motion. While shoulder injuries can occur in all types of overhead throwing athletes, including quarterbacks, tennis players, swimmers, volleyball players, and water polo players, professional baseball pitchers are especially prone to shoulder injuries (1). In fact, 57% of professional baseball pitchers will experience shoulder pain during their careers (2). Additionally, shoulder injuries are the most common injuries in amateur and professional baseball players and result in the most total days of pitching missed (3, 4).

Diagnosing the cause of shoulder pain in overhead throwing athletes can be challenging for a variety of reasons. Pain is often due to overuse from a complex throwing mechanism and the actual inciting event may be difficult to pinpoint. Moreover, many different types of injuries, or a combination of multiple injuries, can manifest in similar symptoms (1). For these reasons, this topic is important to understand for sports medicine physicians, orthopaedic surgeons, and musculoskeletal radiologists.

During pitching, the thrower must generate high energy levels to reach peak acceleration and velocity. During deceleration and after ball release, the forces must then dissipate through the stabilizing structures of the shoulder (5–8). Because of these complex biomechanical forces, a number of structures, including the glenoid labrum, the glenohumeral joint capsule, humerus, rotator...
cuff tendons, muscles, and upper extremity vessels and nerves can potentially be injured, leading to the thrower's pain (1, 5, 9-18).

To our knowledge, the location of where most pitchers experience their pain has not been reported. However, in our experience, acute onset of predominantly posterior shoulder pain occurs in only a small number of these athletes. The most commonly encountered etiologies for posterior shoulder pain in an overhead thrower include posterior muscle strains, internal impingement, which consists of posterior glenoid labral injuries and rotator cuff tendon tears, glenohumeral internal rotation deficit (GIRD), scapular dysfunction, or referred pain from cervical spinal injuries. Occasionally, unusual injuries can be associated with predominantly posterior pain in overhead throwers.

We describe four professional baseball pitchers, each presenting with acute onset posterior shoulder pain while throwing and subscapularis inferior bundle edema along its musculotendinous junction seen on magnetic resonance imaging (MRI) that was felt to represent the main site of recent injury.

Case Report

Methods

Between 2006 and 2015, four professional baseball pitchers, ages 22, 25, 24 and 33, presented to the team’s orthopaedic surgeon with acute onset of posterior shoulder pain that developed while pitching. Routine MRI of their symptomatic shoulders was performed within 7-10 days of initial injury. MRI was performed either on 1.5 tesla (T) magnets (Aera, Siemens, Erlangen, Germany) (Symphony, Siemens, Erlangen, Germany) or 3 T magnets (Verio, Siemens, Erlangen, Germany) (Skyra, Siemens, Erlangen, Germany). Routine shoulder MRI pulse sequences were obtained in axial, sagittal and coronal planes with respect to the glenoid fossa utilizing T1-weighted, proton density, and fluid-sensitive sequences. Because our routine shoulder MRI protocol changed during the time period in which these cases were collected there is some variability in the imaging protocols used in the MRIs of these patients. We have provided our current protocol on Siemens 3 T magnets (Table 1). The studies were each interpreted by a fellowship-trained musculoskeletal radiologist and reviewed with the referring orthopaedic surgeon at the time of exam completion. Once a pattern of findings was identified within this set of patients, the clinical presentation and imaging features of each study were again reviewed by 2 fellowship-trained musculoskeletal radiologists (9 and 5 years of experience respectively), a musculoskeletal radiology fellow, and the referring team orthopaedic surgeon (24 years of experience). The case presentations are summarized in Table 2. The study was granted an internal review board waiver by the institutional ethics committee because no experimental diagnostic modalities were used.

Table 1. Routine MRI Shoulder Protocol on Siemens 3T Scanners

<table>
<thead>
<tr>
<th>Sequence</th>
<th>FOV</th>
<th>Matrix/NEX</th>
<th>ST</th>
<th>TR</th>
<th>TE</th>
<th>FA</th>
<th>ETL</th>
<th>BW</th>
</tr>
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<tbody>
<tr>
<td>Axial T2***</td>
<td>12-16</td>
<td>320x256/2</td>
<td>3</td>
<td>3,000-4,000</td>
<td>50-70</td>
<td>140</td>
<td>12-16</td>
<td>200-300</td>
</tr>
<tr>
<td>Sagittal T2***</td>
<td>12-16</td>
<td>320x256/1 (with 100% oversampling)</td>
<td>3</td>
<td>3,000-4,000</td>
<td>50-70</td>
<td>150</td>
<td>12-16</td>
<td>200-300</td>
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<tr>
<td>Coronal T2***</td>
<td>12-16</td>
<td>320x256/1 (with 100% oversampling)</td>
<td>3</td>
<td>3,000-4,000</td>
<td>50-70</td>
<td>150</td>
<td>12-16</td>
<td>200-300</td>
</tr>
</tbody>
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*Field-of-view; †Number of excitations; ‡Slice thickness; §Repetition time (msec); ‖Echo time (msec); ¶Flip angle; ||Echo Train Length; *Bandwidth; ‡Fat-suppressed; ***Nonfat-suppressed
Case Presentation 1

The first patient was a 22-year-old, right hand dominant, professional baseball pitcher with 3 years of experience. The pitcher reported gradual worsening of shoulder achingness and soreness with pitching over his first four games of the season. He also noted loss of speed and accuracy. After an acute exacerbation during his fourth start, the patient reported new onset of shoulder pain that he felt was located posteriorly and was separate from his prior, vaguer symptoms. The pitcher could not recall a specific inciting event. Additionally, the pain was unrelated to arm positioning or phase of throwing. Physical examination by the team orthopaedic surgeon was negative for tenderness to palpation. Strength testing of the affected arm revealed no loss of strength. Reduced internal rotation was noted with asymmetrically decreased internal rotation to the T6 level on...
the symptomatic side compared to internal rotation to the T6 level on the asymptomatic side. A routine shoulder MRI was performed and demonstrated a focal inferior subscapularis muscle partial tear and edema at the musculotendinous junction, 1 cm medial to its humeral attachment with additional fascial edema extending toward the axilla (Figure 1a). Although a small focal posterior glenoid labrum tear with partial detachment was noted from the posterior 8-10 o’clock positions, this was felt to be a finding that was unrelated to his acute discomfort as there was no significant bone marrow or soft tissue edema around the labral tear, and the adjacent articular cartilage was preserved (Figure 1b). The patient was treated with 10 days of rest and nonsteroidal anti-inflammatory medication. The pitcher was also instructed to follow a stretching and rehabilitation throwing program. Following this course of therapy, there was a gradual resolution of pain. Shortly thereafter, the pitcher returned to normal function and regained normal strength/velocity.

Case Presentation 2

The second patient was a 25-year-old, right hand dominant, professional baseball pitcher with 4 years of experience. The pitcher experienced an acute shoulder injury during off-season throwing. He complained of posterior inferior shoulder soreness that radiated to the posterior axillary line following the shoulder injury. The patient could not correlate the injury with a particular arm position or phase of throwing. The physical examination performed by the same team orthopaedic surgeon was negative for tenderness with palpation or loss of strength. Additional orthopaedic tests were negative and the etiology of the pain was unclear. A routine shoulder MRI was performed and demonstrated a grade 2 subscapularis inferior bundle muscle strain, and the site of the tear and surrounding fascial edema were adjacent to the axillary neurovascular bundle (Figure 2a). There was moderate supraspinatus tendinosis and a 2 mm partial-thickness, articular surface tendon tear, both of

Figure 2. 25-year-old, right hand dominant professional baseball player with an acute shoulder injury during off-season pitching: (a) Coronal T2-weighted TSE FS image of the anterior right shoulder shows a partial-thickness tear at the subscapularis musculotendinous junction (arrow). Note high signal intensity in the affected region. Additionally, the axillary neurovascular bundle is seen in close proximity to the site of this tear (arrowhead), (b) Coronal T1-weighted spin echo (SE) FS MR arthrogram image of the same shoulder at the level of the anterior supraspinatus tendon shows contrast undercutting the articular surface of the tendon (arrow), consistent with partial-thickness, articular surface tendon tear.
which were unchanged dating back at least 2 years (Figure 2b). No additional pertinent findings were seen. The team orthopaedic surgeon treated the patient for a muscle strain with ice and off-season rest. An off-season rehabilitation throwing program was also instituted. Following the course of therapy, the player noted resolution of pain. The pitcher fully recovered his function by the time the start of the next season began.

Case Presentation 3

The third patient was a 24-year-old, right hand dominant, professional pitcher with 4 years of experience. The player experienced an initial onset of burning posterior shoulder pain after throwing a fastball in the 3rd inning of a regular season game. He continued to have posterior pain and achiness with throwing through the 6th inning when he was finally substituted. The patient was unable to pinpoint a time in his throwing cycle when he injured his shoulder. Additionally, the pain was unrelated to arm position during throwing. The team orthopaedic surgeon identified posterior shoulder soreness with abduction and external rotation. There was also reduction in the pitcher’s internal rotation to the T6 level on the symptomatic side compared to the T4 level on the asymptomatic side. No tenderness on palpation was present on physical examination, and further shoulder testing for rotator cuff or labral tears was also negative. A routine shoulder MRI was performed and demonstrated a focal partial-thickness tear of the inferior subscapularis musculotendinous junction (Figure 3a). There was additional fluid tracking along the anterior surface of the muscle toward the axilla. No additional rotator cuff or labral abnormality was seen. The patient was treated in a similar fashion to the previous two pitchers who were felt to have symptomatic inferior subscapularis muscle strains, including ice and 10 days of rest. He was given an additional course of oral steroids. The player also gradually returned to

Figure 3. 24-year-old, right hand dominant professional baseball pitcher with posterior shoulder pain after throwing a fastball: (a) Sagittal T2-weighted TSE FS MR image of the right shoulder shows a focal partial tear of the inferior subscapularis musculotendinous junction (arrow) and additional fluid tracking along the anterior surface of the muscle toward the axilla. Note high signal intensity in the affected region, (b) Sagittal T2-weighted TSE FS image of the same shoulder from a follow-up MRI 6 weeks after starting a course of conservative treatment, showed improvement in the inferior musculotendinous subscapularis muscle edema (arrow), consistent with resolving injury. Note decreased high signal intensity in the affected region.
activity with a rehabilitation throwing program. The patient noted mild improvement of symptoms for a brief period, but had a relapse injury 6 weeks later while warming up before a game. A follow-up MRI was then performed and showed mildly progressive inferior subscapularis musculotendinous partial-thickness tear (not shown). No other acute abnormality was seen. Once again, the patient was treated for an exacerbation of a muscle strain with conservative therapy. A second follow-up MRI examination 6 weeks later was performed and showed significant decrease in the inferior musculotendinous subscapularis muscle edema, consistent with resolving injury (Figure 3b). Over the remainder of the season, the pitcher experienced gradual resolution of pain and returned to normal function.

**Case Presentation 4**

The final, most recent patient was a 33-year-old, right-hand dominant professional baseball pitcher with 7 years of experience. The pitcher experienced acute onset of progressive posterior shoulder pain while warming-up prior to entering a game. Similar to the prior cases the patient could not identify a phase of the pitching cycle in which the in-

![Figure 4. 33-year-old, right hand dominant professional baseball pitcher with posterior shoulder pain experienced during warmups:](image-url)

(a) Sagittal T2-weighted TSE FS MR image of the right shoulder shows a focal partial tear in the region of the subscapularis musculotendinous junction (arrow) and additional fluid tracking along the anterior surface of the muscle toward the axilla. Note high signal intensity in the affected region, (b) Sagittal T1-weighted nonfat-suppressed MR image of the same shoulder demonstrates moderate inferior subscapularis muscle fatty atrophy (arrow). (c) Axial T2-weighted TSE FS MR image of the same shoulder on a preseason MRI performed 8 months prior depicts a posterior labral tear (arrow). The patient was asymptomatic at the time of initial MRI.
jury occurred, and the symptoms did not worsen in particular positions or with certain movements. The patient had suffered a shoulder strain 5 years prior that was treated with rest followed by a program of physical therapy, and was able to recover full function. Physical examination revealed weakness with shoulder abduction and a deficit in internal rotation, but was negative for tenderness to palpation. Additional testing for rotator cuff or labral pathology also was deemed negative. A routine shoulder MRI was performed and demonstrated a focal partial-thickness tear of the inferior subscapularis musculotendinous junction (Figure 4a). There was additional fluid tracking along the anterior surface of the muscle toward the axilla. There was moderate inferior subscapularis muscle fatty atrophy (Figure 4b). Of note, the patient had a preseason MRI examination 8 months prior demonstrating a posterior labral detachment at the posterior 9 o’clock position (Figure 4c), but was asymptomatic at that time. On the repeat MRI examination, the detachment was inconspicuous, suggesting healing (not shown). No additional rotator cuff or labral abnormality was seen. The patient was again treated conservatively for muscle strain, including off-season rest and gradual return to overhead throwing with a rehabilitation program. He has noted significant reduction in his discomfort.

Discussion

Although shoulder pain is common in overhead throwing athletes, acute onset of predominantly posterior shoulder pain seems uncommon. Posterior shoulder pain in these patients is typically the result of high stresses placed on the internal structures of the shoulder with alteration of biomechanics due to repetitive, forceful throwing (13, 19). The commonly encountered etiologies of posterior shoulder pain include internal impingement with posterior rotator cuff strains or tendon tears, and posterior labro-capsular injuries, or GIRD (11, 13, 20, 21).

Posterior rotator cuff pathology is typically due to degeneration of the cuff from the extreme repetitive forces generated during pitching (22). The most common locations for injury include the undersurface of the posterior half of the supraspinatus and anterior half of the infraspinatus tendon (23). Imaging findings range from tendinosis, to partial-thickness and full-thickness rotator cuff tendon tears (24, 25).

Internal, or posterior, impingement is a mechanism that has been proposed for the cause of a spectrum of injuries in the overhead throwers that includes posterolateral humeral head subcortical edema and pseudocyst formation, posterior labral fraying/tearing, and partial-thickness articular surface rotator cuff tendon tears (24, 26, 27). Impingement occurs during the late cocking phase of throwing when the arm is in abduction, external rotation, and extension. This positions the posterior superior labrum between the greater tuberosity of the humeral head and the posterior rotator cuff, which places these structures at risk for injury (13, 19).

The propensity for posterior glenoid labral tears in throwers is believed to be the result of tightening of the posterior band of the inferior glenohumeral ligament (IGHL), as a result of repetitive tensile forces during the follow-through phase of throwing (13). A contracted posterior band of the IGHL shifts the humeral head contact point on the glenoid and results in GIRD. This ultimately allows hyper-external rotation, which leads to increased torsional forces transmitted through the biceps labral complex (BLC), resulting in SLAP type II posterior superior labral lesions (13, 28). The changes seen with GIRD are initially adaptive in overhead throwers and allow for the generation of greater throwing forces. In fact, many professional overhead throwing athletes exhibit
physical examination findings of GIRD even if they do not experience findings often seen in symptomatic GIRD, which includes progressive/chronic shoulder pain and achiness that is frequently posteriorly located, along with decreasing throwing velocities (13). It is possible the alterations in biomechanics experienced with GIRD, such as the posterosuperior shift of the humeral head, could increase strain on anteroinferior supporting structures, such as the inferior bundle of the subscapularis muscle, and predispose these athletes to subscapularis injuries.

To our knowledge, subscapularis muscle injury as the cause of posterior shoulder pain in adult overhead throwing athletes has not been previously reported. A literature search revealed two solitary case reports and one case series of subscapularis injuries causing shoulder pain in baseball players. One report described a case of subscapularis muscle strain that an outfielder endured from direct impact against a wall (15). A second case reported spontaneous subscapularis tendon rupture in a 50-year-old patient playing recreational baseball who experienced sudden pain after forcefully throwing a ball to a catcher from second base (29). This particular patient reported anterior shoulder pain. A third, more recent case series by Polster et al. described 11 baseball players with muscle strains involving the inferior half of subscapularis at musculotendinous junction (30). However, the case series included both pitchers and non-pitchers, and none of the cases reported a clinical history of posterior shoulder pain. Additionally, the series did not discuss whether the injuries were isolated.

We have found four professional baseball pitchers presenting with acute posterior shoulder pain while throwing, with unexpected subscapularis inferior bundle musculotendinous junction strains diagnosed on MRI. Similar to the work by Polster et al. the common finding in each of the four athletes was muscle edema within the inferior bundle of the subscapularis muscle at the musculotendinous junction, suggesting a low-grade muscle strain. The soft tissue edema also extended into the axilla along the inferior glenohumeral ligament.

In one of the four patients, no additional findings to explain the etiology of the patient's pain were seen. Specifically, there was no injury to the supraspinatus or infraspinatus muscles or tendons, MRI findings of internal impingement, or posterior labral pathology. The imaging of another of our patients did show moderate supraspinatus tendinosis with a small partial-thickness articular surface tendon tear. However, these findings were unchanged dating back 2 years, and therefore felt unlikely to be the source of acute pain. In the third patient, there was a small posterior labral detachment. However, the labral injury was not believed to be the cause of the patient's acute shoulder pain as there was no associated bone marrow edema to suggest an acute event, nor was there underlying glenoid articular cartilage loss that could explain posterior shoulder pain with throwing.

In the most recent case the patient had a posterior labral detachment seen on a preseason MRI examination 8 months prior. However, the patient was asymptomatic at that time, and on the subsequent study demonstrating a subscapularis musculotendinous strain, the labral tear was no longer visible suggesting healing. In addition to the acute subscapularis strain, there was inferior subscapularis muscle atrophy, likely related to a remote muscle strain sustained while pitching 5 years earlier, suggesting a recurrent or acute on chronic injury. Finally, although at least three of our patients demonstrated clinical findings of GIRD, which often does present with posterior shoulder pain, the patients presented with abrupt onset of pain that was either new or felt to be different in quality to existing symptoms. The sudden onset of symptoms is atypical of
GIRD but more commonly seen with musculotendinous injuries.

The findings of each study were reported to the team orthopaedic physician at the time of the exam, who agreed with the diagnosis of subscapularis inferior bundle muscle strain at the musculotendinous junction as the cause of the patients’ posterior shoulder pain. The patients were treated conservatively with rest followed by a throwing rehabilitation program, and their symptoms improved within several weeks. No further potential etiologies for the pitchers’ pain were detected in the subsequent weeks following presentation. Although three of the patients performed at a pre-injury baseline level for a substantial length of time following treatment, one of the patients did demonstrate gradual decline in function the following season. However, this was favored to be due primarily to the development of throwing shoulder microinstability and rotator cuff fatigue, with the subsequent development of rotator cuff tears.

While not frequently injured in overhead throwers, the subscapularis muscle, like the other rotator cuff muscles, has a dynamic role in pitching and experiences strong forces during the violent throwing motion (15, 31). The subscapularis muscle serves multiple functions in shoulder stabilization and motion. Its major roles include internal rotation, shoulder abduction, humeral head depression, and anterior stabilization (17, 18). During pitching, the subscapularis muscle begins eccentric contraction during the late cocking stage to halt external rotation while applying an anterior stabilization force to the glenohumeral joint (31, 32). The muscle reaches its maximal activation during the acceleration phase of throwing, contributing to violent internal rotation (16). Internal rotation forces reach as high as 185% of its maximum muscle strength, while internal rotation angular velocities can be as high as 7000 to 9000 degrees per second (16, 28, 31).

The mechanism of inferior subscapularis musculotendinous junction muscle injury in this group of throwing athletes is not entirely clear. Subscapularis injuries in general have mostly been described in the setting of rotator cuff tendon tears, as these would be more surgically relevant. Rotator cuff tears involving the subscapularis muscle are far less common than those involving the supraspinatus and infraspinatus muscles (33). When the subscapularis tendon is torn, it usually occurs in conjunction with supraspinatus tendon tears (34). Subscapularis tendon tears are typically degenerative (35). Although when acute traumatic tears do occur, they predominantly occur in younger patients (36).

The most common mechanism of injury of the subscapularis tendon is in the setting of external rotation (36). The greatest forces exerted on the musculotendinous complex occur in the setting of hyper-external rotation and abduction, when the subscapularis is maximally stretched during eccentric contraction (35). This occurs during the late cocking phase of throwing. However, it has recently been shown that throwers with a shorter arc of motion are more likely to experience subscapularis strains, suggesting that the greater angular acceleration and power generated by the subscapularis in the early acceleration phase may be the major contributing factor to injury (30). Either way, it is likely that these massive forces exerted on the subscapularis during extreme external rotation and by the subscapularis during powerful acceleration are major factors in subscapularis injury in the setting of pitching.

The subscapularis muscle is composed of two functionally independent bundles with separate nerve innervations, the upper and lower subscapular nerves which originate from the posterior cord of the brachial plexus (33, 34). This configuration allows each bundle to achieve different activity lev-
els during muscle activation (34, 37). As a result, the two bundles have different roles during shoulder motion. The lower subscapularis, which is more transversely oriented to the humerus during cocking motion, activates earlier and has greater activity during abduction and flexion (30, 37). Thus, it has a greater role in humeral head depression and resistance to anterior translation (37). The differences in the roles of the two bundles may help explain why the inferior bundle is more prone to injury that could occur during the late cocking hyper-external rotation/abduction phase.

The clinical presentation of subscapularis injuries varies depending on the mechanism of injury. The pain experienced in subscapularis musculotendinous injuries is typically more anterior than the pain experienced in other rotator cuff tears (35, 38). Additionally, patients with subscapularis injuries may present with night pain and shoulder weakness (37). Physical exam findings may demonstrate anterior shoulder tenderness, increased passive external rotation, and weakness with internal rotation, which can be tested by the subscapularis lift off test, subscapularis lag sign, and subscapularis belly press test or strength test (11, 35, 38).

The cause for posterior pain in our cohort is uncertain. Since the muscle and its musculotendinous junction are anterior structures, the sensation of posterior pain is unlikely to originate from the subscapularis itself. For this reason, it is postulated that the posterior pain from this injury is a referred pain caused by local irritation or stretching of nerves, which course along the site of injury. In each of our cases, soft tissue edema tracked along the musculotendinous junction toward the axilla, and is in close proximity to neurovascular bundles.

In particular, there are two nerves that are possible candidates for causing referred pain in the setting of subscapularis inferior bundle muscle strain. One candidate, the axillary nerve, courses near the inferior margin of the inferior glenohumeral ligament. The posterior branch of the axillary nerve gives rise to the superior lateral cutaneous nerve, which is a sensory nerve that supplies the skin over the lower two/thirds of the posterior deltoid. The second candidate is the radial nerve, which courses along the posterior wall of the axilla on the subscapularis muscle. The nerve directly gives off a posterior sensory branch, the posterior cutaneous branch of the radial nerve, which supplies the skin over the posterior upper arm and forearm. Of the two potential causes of referred pain, the posterior sensory distribution of the superior lateral cutaneous nerve branch more closely corresponds to the reported site of pain in this cohort. Therefore, referred pain from irritation of the axillary nerve as it courses alongside edematous soft tissues tracking toward the inferior glenohumeral ligament could result in the sensation of posterior shoulder pain in the setting of subscapularis inferior bundle strain.

**Conclusion**

While uncommon, inferior subscapularis musculotendinous junction strains do appear related to the symptom of acute onset posterior shoulder pain in our cohort of professional baseball pitchers. This injury is likely related to the violent mechanism of throwing, with extreme stretching of tendon fibers during hyper-external rotation and abduction, and extreme force generation during rapid acceleration of the arm through its arc of motion. While the exact etiology of the posterior pain is uncertain, it could be the result of local irritation of the axillary nerve and referred pain from its superior lateral cutaneous branch. Knowledge of this association in overhead throwing athletes, along with the signs and symptoms during presentation, may be helpful to clini-
cians to make the diagnosis and implement appropriate treatment more quickly.

What Is Already Known on this Topic
Very few published reports of subscapularis injuries in baseball players exist. 2 are case reports, one in a player with direct trauma and the other in an older, amateur player. There has been one case series by Polster et al. in 2016 on subscapularis injuries in baseball players. However, this work does not directly address the location of presenting symptoms.

What this Study Adds
Although pitchers with posterior shoulder pain may most commonly present with posterior labrocapular or posterior rotator cuff injuries, our work tries to highlight an injury to an anterior/inferior structure, the subscapularis muscle and tendon, that may seem somewhat remote from the site of presenting symptoms. As a result, this finding was initially surprising both to the referring orthopaedic surgeon and interpreting radiologist. To our knowledge this is the first description of this injury pattern presenting with posterior shoulder pain.

Authors’ Contributions: Conception and design: IMO, EMT and SMG; Acquisition, analysis and interpretation of data: IMO, EMT, KJB and SMG; Drafting the article: EMT and IMO; Revising it critically for important intellectual content: IMO, EMT, KJB and SMG; Approved final version of the manuscript: IMO, EMT and SMG.

Conflict of Interest: The authors declare that they have no conflict of interest.

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