

CASE STUDY – MSK injections course (Module 1)

Subacromial Bursitis and Impingement

This case study refers to a patient I saw in the radiology department alongside my supervisor, a musculoskeletal ultrasound accredited ESP.

I selected this case because she was a relatively young patient with a serious medical problem and multiple considerations to weigh up in deciding best management and ensuring we did not exacerbate issues for her.

Patient:

49 year old female diagnosed with metastatic cancer of unknown primary 6 months previously following two months of lethargy, right loin pain and night sweats. A CT KUB had been performed in the emergency department in view of the loin pain which had incidentally found her cancer.

Unfortunately, the cancer was disseminated at presentation with widespread metastases, including to her liver, spleen, peritoneum, right lung, axillary/supraclavicular/cervical lymph nodes, intramuscular and the proximal humeri.

Histological diagnosis and further CT/PET scanning resulted in a likely diagnosis of cholangiocarcinoma or sarcoma. She was subsequently commenced on single agent chemotherapy but sadly her disease continued to progress despite this. Following this, further genetic testing suggested malignant melanoma as the highly likely primary. The patient had lived in south Africa as a child before living in California for 20 years and had undergone numerous skin lesion excisions/freezing.

The genetic results indicated probable susceptibility to a particular checkpoint inhibitor and therefore targeted immunotherapy (ipilimumab and nivolumab) was commenced which has been successful in halting disease progression and shrinking some metastases. Other medication consisted of codeine, naproxen and omeprazole currently. Her rheumatologists were hoping to avoid oral steroid therapy due to its effect on her immunotherapy.

This lady had been referred by her GP for an out-patient USS of both shoulders and possible injection depending on findings. She had developed increasingly severe pain in both shoulders over the preceding 3 weeks as well as deep muscle aches around her pelvic girdle/proximal quadriceps muscles. She was hardly able to move her right shoulder due to

pain and left shoulder was very painful to abduct beyond around 20 degrees. She was finding this very disabling and was frequently woken from sleep by the pain. The presumed diagnosis was inflammatory arthritis as a side effect of the immunotherapy agent.

In view of this patient's medical history; Inflammatory arthritis due to immunotherapy was a possible differential in addition to pain from the bony metastases in bilateral proximal humeri or referred pain. Hypercalcaemia as a cause of bony pain had already been excluded by her oncology team. Degenerative change was unlikely based on patient age, Xray and ultrasound findings. Polymyalgia rheumatica was still a possibility but her ESR was not unduly raised.

Musculoskeletal effects of immunotherapy:

Immunotherapy is a relatively recent advance in the management of several cancers, including metastatic melanoma that has conveyed a dramatically improved survival benefit to patients eligible for this treatment. Suitability depends on genetic results as immunotherapy involves biological agents that target immunological checkpoints, e.g. PD-L1 (programmed cell death ligand 1). These checkpoint inhibitors work by suppressing/regulating pathways and hence boosting immune response to tumours.

Immunotherapy is unfortunately accompanied by a spectrum of immune-related adverse events (irAE's), essentially initiation of autoimmune disease brought about by over-activation of the immune system. However, rheumatic complaints have been reported far less frequently than the more common GI/dermatological and endocrine as most clinical trials have not reported on resultant MSK complaints.

Cappelli *et al* described inflammatory arthritis and sicca syndrome in 13 patients receiving nivolumab and/or ipilimumab.² In this report, they described nine patients who developed inflammatory arthritis; synovitis was confirmed by imaging in four.

In general, irAEs have been reported to be steroid sensitive and in most cases resolve within 6–12 weeks.

Many did not however and it is important to get on top of MSK pain, with the risk being that patients may be taken off the immunotherapy or have to take additional anti-TNF drugs which caused more aggressive immune suppression.

Ultrasound Scan:

This was performed using a linear probe on a GE logiq machine (GE LOGIQ E9 R6 xDClear 2.0). A MSK preset was utilised.

On examination of her right shoulder, active and passive movement was significantly reduced in all planes, with virtually no external rotation possible.

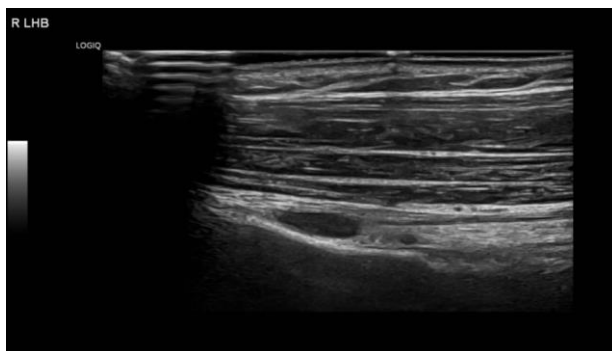
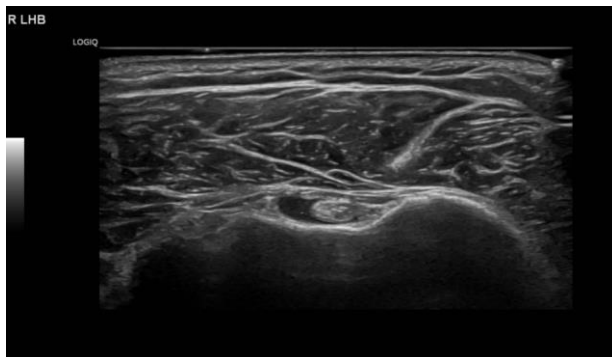
Ultrasound showed a tendon sheath cyst with no internal vascularity on colour doppler. Rotator cuff tendons were intact as far as sub-optimal positioning allowed us to ascertain. There was mild subacromial-subdeltoid (SASD) bursa thickening but no other positive findings. In light of the ultrasound findings and her restricted joint ROM, the likely diagnosis was thought to be adhesive capsulitis. She was therefore referred for a shoulder hydrodilatation with the consultant radiologist.

The left shoulder was a lot more mobile but there was a clear painful arc beyond 20 degrees abduction/flexion consistent with impingement and tenderness over the anterior gleno-humeral joint.

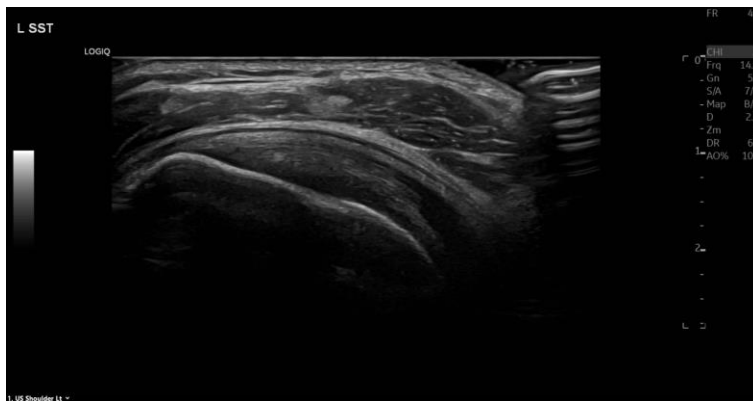
Ultrasound demonstrated no evidence of joint effusion and all rotator cuff tendons appeared intact. The only positive finding on ultrasound was of moderate thickening of the subacromial subdeltoid (SASD)bursa suggesting bursitis.

Images:

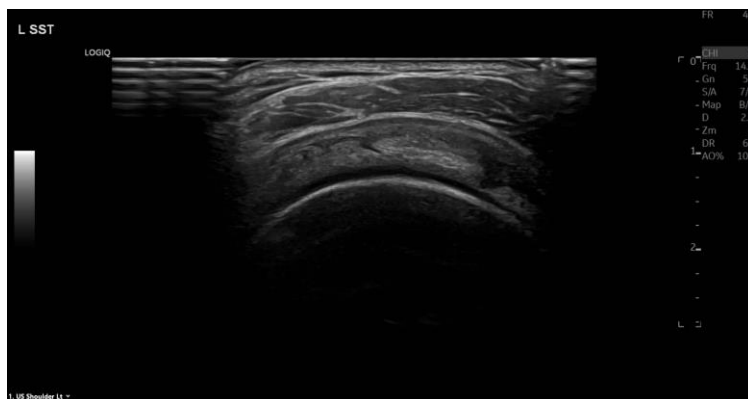
Right shoulder – biceps tendon sheath cyst



Left shoulder – moderate thickening of the sub-acromial sub-deltoid bursa. Supraspinatus tendon intact and no evidence of tendinopathy. Dynamic assessment demonstrated some bunching of the supraspinatus tendon on abduction of her arm, suggesting impingement (in the presence of a painful arc).



Longitudinal view supraspinatus tendon



Transverse view supraspinatus tendon

I focussed on the left shoulder SASD bursitis since this is the complaint we addressed in this outpatient appointment by offering a steroid injection at a later date.

Role of ultrasound in this diagnosis:

Sub-acromial impingement has been defined as a clinical syndrome of antero-lateral shoulder pain and a mid-range painful arc during elevation of the arm. Much of the shoulder pain experienced in this situation, is often thought to be due to inflammation within the sub-acromial bursa. Its diagnosis is challenging due to the variable nature of presentation (e.g. may present with crepitus) and a range of conditions that may elicit similar symptoms. The general consensus is that this classic painful arc is caused by

compression of the rotator cuff and/or SASD bursa by the coraco-acromial arch (Read 2010).

The most obvious benefit ultrasound has over MRI in the diagnosis of this condition is that it allows dynamic evaluation of the joint as the arm is abducted.

Potential ultrasound features of SASD bursitis/impingement:

- Bunching or fluid distension of the supraspinatus tendon lateral to the impingement point at the coraco-acromial arch.
- Bulge of the coraco-acromial ligament
- Migration of humeral head cranially

However, ultrasound alone is not accurate in diagnosing this condition as bursal bunching is frequently found in around a third of asymptomatic shoulder and may be absent in a fifth of shoulders displaying impingement symptoms. (Read 2010).

Combined with clinical examination, with elicitation of the painful arc; positive ultrasound findings as noted above vastly improves its diagnostic accuracy.

Ultrasound is operator dependent so you would expect variability in diagnostic accuracy with this modality. A study in 2016 however found excellent overall agreement when scanning 46 sports men/women (around 50% symptomatic) and diagnosing sub-acromial pathology. This was particularly high for assessment of dynamic impingement (overall agreement was 98% and 93%, with Kappa of 0.96 and 0.82, for intra- and inter-rater reliability) (Birgitte 2017).

Essentially ultrasound (particularly when combined with clinical examination and dynamic assessment is an excellent diagnostic modality for sub-acromial bursitis and impingement. It is accessible, cheap, low risk and allows for guided injections to be performed safely.

MRI is also frequently used in these cases and despite being a static modality; it does confer some advantage over ultrasound in situations whereby the impingement is brought about by acromio-clavicular osteoarthritis or due to the shape of the sub-acromial space. (El-Shewi 2019). Xray may also be useful in detecting such bony degenerative changes, which were absent in this case.

Justification for injection:

This patient was very unwell with terminal cancer but managing relatively well on immunotherapy to prolong her life and slow progression of disease. The main complaint she had currently was the bilateral shoulder pain which she described as incapacitating and prevented her from lifting up her 4 year old daughter.

In view of her complex medical history, other possible contributors to shoulder pain (muscle wasting and bony metastases), immunotherapy medication and wish to do no harm; the patient was asked to return the following week for the bursal injection of her left shoulder so we had time to look at the evidence for this and discuss with senior radiologists/her rheumatology and oncology team. With immunotherapy being a relatively novel treatment still, we felt it best to approach this as a multi-disciplinary team.

Our main concern would be weighing up risk versus benefit in a person on immune modulating drugs who may be at higher risk of infection, in whom it may have little benefit and whom may suffer from a more severe post injection flare.

The patient's rheumatology team and oncology team were both in favour of bursal injection and hydrodilataion to try and improve the patient's quality of life and allow her to tolerate these potential side effects of immunotherapy and continue taking this life prolonging medication. It could also potentially reduce the need for more disruptive systemic steroid therapy if the injection obviated the need for oral prednisolone to calm down generalised inflammatory effects.

Immunotherapy:

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Immunotherapy is unfortunately accompanied by a spectrum of immune-related adverse events (irAE's), essentially initiation of autoimmune disease brought about by over-activation of the immune system. However, rheumatic complaints have been reported far less frequently than the more common GI/dermatological and endocrine as most clinical trials have not reported on resultant MSK complaints (Shen 2021).

Cappelli *et al* described inflammatory arthritis and sicca syndrome in 13 patients receiving nivolumab and/or ipilimumab.² In this report, they described nine patients who developed inflammatory arthritis; synovitis was confirmed by imaging in four.

Evidence for SASD bursal injection:

In general, studies show that irAEs have been reported to be steroid sensitive and in most cases resolve within 6–12 weeks.⁸

Many were not however and it is important to get on top of MSK pain. The risk of not doing so is that patients may be taken off the immunotherapy or have to take additional anti-TNF drugs which caused more aggressive immune suppression.

During the pandemic, the British Society for Rheumatology and many similar organisations released a consensus statement stating “Only consider a steroid injection if a patient has failed first line measures, has high levels of pain and disability, and continuation of symptoms will have a significant negative effect on their health and wellbeing.” Though this was pre-vaccine availability and advice is likely to have changed since, I feel this patient would have still fitted their criteria for injection (BSR Nov 2020).

Systematic reviews (including a Cochrane review) of treatments for subacromial pain, subacromial impingement, and rotator cuff syndrome have concluded that corticosteroid injection has an advantage over more conservative approaches such as NSAID’s, acupuncture, ice and physiotherapy. Though physiotherapy has an important role too, it is usually beneficial to have an initial steroid injection to reduce inflammation and allow increased range of movement, reduced pain and therefore ability to undertake the advised exercises (Stephens 2008).

Blind versus ultrasound guided injections:

A large systematic review and meta-analysis investigated the efficacy of ultrasound guided versus landmark based corticosteroid injections into the SASD bursa in adults with shoulder pain. It reviewed 7 papers with a total of 445 patients and an approximate 50:50 split between the two approaches to injection (Wu T 2015).

It demonstrated a clear statistically significant advantage for the ultrasound guided technique in its 4 different outcome parameters of pain score, shoulder function score, shoulder abduction range of motion and in injection efficacy at 6 weeks.

This is not surprising since a large proportion of unguided injections are known to miss the intended target. An interesting study in 2019 used cadavers to compare guided versus unguided injections around the shoulder joint with intended target of the supraspinatus tendon sheath. 240 punctures by 30 clinicians experienced in MSK ultrasound were performed (50:50 of each technique). Unguided punctures were on average of 10mm further away from their target than the US guided punctures. Precision rates for US guided procedures were 95 % compared with 12.5% for blind techniques ($p < 0.0001$) (Abat 2019).

Injection technique:

A 5–12 MHz linear array transducer was used on the GE logiq machine. PPE including sterile gloves, mask and apron were worn throughout.

The machine was cleaned thoroughly with Clinell wipes before use; particularly important with a shielding patient.

The patient sat facing away from me on a stool with her left hand resting on her left hip. After establishing there were no known allergies; her shoulder was cleaned several times with chlorprep and allowed to dry.

Following a preliminary scan to confirm previous findings; the sterilised transducer in a sterile probe cover was placed transversely over the supraspinatus tendon so that the sub-acromial bursa was visible just beyond the acromion. No gel was used but the covered probe dipped in sterile solution.

An in-plane technique was used with the 21G needle inserted, bevel-down, at an angle of approximately 45 degrees under ultrasound guidance in an anterior approach. 5ml 1% lidocaine was injected (well below the maximum safe dose of 3mg/kg in this 65kg patient) before taking the syringe off and replacing it with a syringe containing 1ml sterile saline and 1ml depo-medrone (40mg). Free flow of the drugs injected was observed and bursal distension seen on ultrasound.

Since my supervisor was a physiotherapist (with MSK Ultrasound diploma), we had to operate under PGD guidance and therefore were required to do 2 separate injections since no pre-mix was available. He acted as an assistant during the injection to reduce the risk of me contaminating the field.

A corticosteroid was used with the aim of reducing any bursal inflammation (as suggested by bursal thickening) due to their inflammatory modulating effect. They achieve this by their direct action on nuclear steroid receptors to control mRNA synthesis rate and their effect on reducing the amount of pro-inflammatory mediators such as cytokines (Resteghini).

Depo-medrone (Methylprednisolone acetate) was selected because it is relatively potent and non-fluorinated. The latter property gives it a lower risk of tendon rupture from collagen atrophy than fluorinated compounds such as Kennalog (Triamcinolone acetonide). Depo-medrone has been found to be the most common choice for sub acromial bursa injections amongst surgeons, sports medicine doctors and rheumatologists (Skedros et al). However, overall evidence for one corticosteroid having any superiority over another is generally lacking and selection is often down to individual preference and familiarity.

Safety and Medico-legal considerations:

- Consent – this is most often verbal in the ultrasound room but a patient should have already received information prior to attending and completed a written form about previous medical problems, medication, allergies etc. Most institutions have recently also added a covid questionnaire to highlight risk to them and staff and consider vaccine timings related to any corticosteroid injections.
- Consent should be voluntary, informed and given by a patient with the capacity to make that decision. Capacity refers to the ability to understand, retain, weigh up and communicate a decision when presented with all relevant information (Mental Capacity Act 2015).
 - An additional consideration in this case is whether the patient has their judgement/understanding clouded by their underlying medical condition. Many patients with disseminated metastatic cancers will have metastases in their brain and once their capacity begins to become impaired by this require their appointed power of attorney to help with these decisions/make them on their behalf. Acute electrolyte disturbances brought about by various treatments/disease processes may also temporarily affect judgement, such as deranged sodium or calcium levels.
 - Having looked in to the above factors and having spoken with the patient; it was clear that she did have capacity.
 - The Montgomery ruling 2015 highlighted the significance of providing all relevant evidence based information to the patient prior to her deciding whether to have the injection or not. Time to mull over this information and consider options are highlighted as important; hence we did not continue with the injection on the same day but brought her back the following week.
- Safety considerations include ensuring no current infection, allergy to the proposed medication or cleaning agent, that the maximum dose of local anaesthetic was not exceeded and that everything possible was done to reduce the risk of infection.
 - Additionally in this case; the patient's immunotherapy treatment and underlying cancer diagnosis had to be considered.
- Although consent-wise, it was appropriate to bring the patient back at a later date to perform the injection; this should be balanced with the risk to a shielding patient of bringing her back to hospital on additional occasions where she then may be at increased risk of covid-19 exposure.
 - A retrospective analysis of 110 patients on immunotherapy alone for cancer treatment examined their risk from covid compared to the general population. Having cancer itself increased the risk of mortality/ICU admission compared with the general population but being on the immunotherapy specifically within this group did not seem to confer any additional risk (Rogiers 2021).

Management plan post injection:

A dressing was applied over the injection site to continue to minimise risk of infection. A patient information leaflet was provided which included information about the possible side effects, safety netting advice and activity modification advice for the first few days post injection. (BSR recommendation)

Possible side effects:

- Flare (in 2-10.7% of people in the few days post injection). This is due to corticosteroid crystals mimicking septic arthritis (Resteghini).
- Skin changes (hypopigmentation and fat atrophy)
- Infection (minimal with good cleaning and technique)
- Facial flushing (<1% on day 2).
- Temporary changes in mood/menstruation

The patient was also asked to remain in the radiology department in view of staff for 20 minutes post injection to allow for any allergic reactions to manifest themselves.

Activity modification would include advice to avoid loading the shoulder for 2-3 days post injection with the aim of maximizing therapeutic effect and preventing excessive spread of the steroid to surrounding tissues. (Molini 2012)

This patient was already fully vaccinated against covid-19 but was yet to receive her booster. Based on current consensus opinion and due to the fact that corticosteroids have been shown to cause hypothalamic-pituitary-adrenal suppression; it was recommended that she avoid the injection for 2 weeks before and 1 week after her booster injection. It was postulated the injection could reduce immunogenicity and therefore vaccine efficacy and an increased risk from coronavirus during that time. (AAOS)

Unfortunately I do not have outcome data for this patient as she has not yet returned for review by rheumatology.

Learning points for me from this case study were:

- The importance of correlating clinical examination findings with radiological findings and symptoms.
- Considerations in who to inject and who not to.
- The value of taking time to evaluate this decision when the medical history is complex and involving a MDT approach when risk/benefit analysis is difficult. This is particularly pertinent when novel immune-modulating therapies are concerned with

little evidence around their interactions currently, plus being in the middle of a pandemic.

- Good clear evidence for ultrasound guided versus blind injection, at least regarding SASD bursal injections.
- The importance of informed consent, shared decision making and documentation of discussions.
- Importance of post procedure advice, including warning patients to possibly expect a flare in the days after.

Word count 3280

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