Letters

IATROGENIC PNEUMOTHORAX FOLLOWING PLATE FIXATION OF THE CLAVICLE

Editor,

A 37-year-old right hand dominant male sustained a comminuted, displaced midshaft fracture of his left clavicle as the result of a motorcycle accident. He did not incur any other injuries. After discussing the treatment options, a decision was taken to proceed with open reduction and plate fixation of his left clavicular fracture. The procedure was performed under general anaesthesia in the beach chair position. A direct incision was made over the left clavicle and the fracture was exposed and reduced. The fracture was stabilised using a pre-contoured titanium plate with a combination of non-locking and locking screws. No concerns were reported in the peri-operative period by the anaesthetic team. A routine check x-ray of the left clavicle was obtained the following day which demonstrated an excessively long medial screw (**Figure 1a**) with a left apical pneumothorax confirmed on a chest radiograph (**Figure 1b**). The patient returned to theatre for insertion of a left-sided chest drain and screw exchange. The pneumothorax resolved and the patient's left clavicular fracture proceeded to complete union.

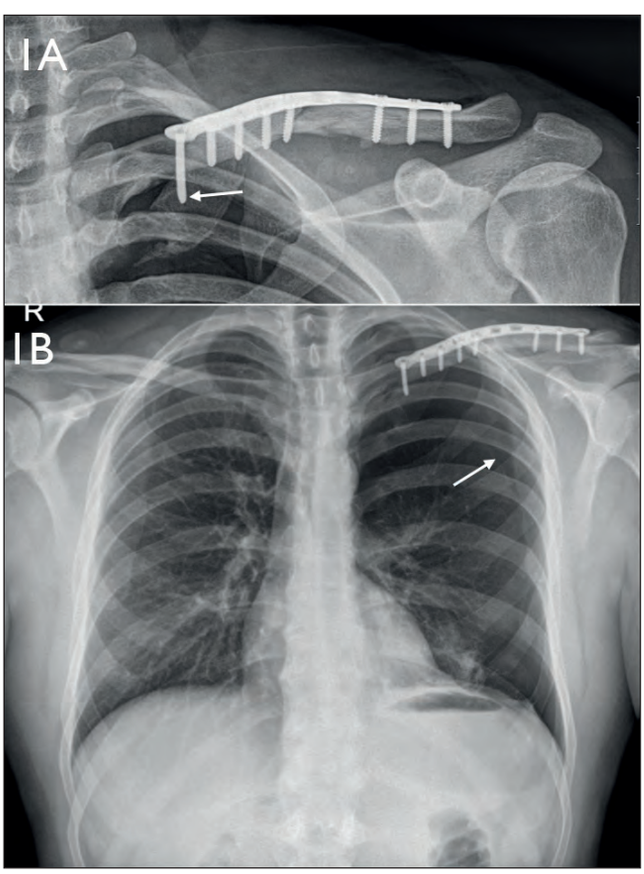

Figure 1a (top): left clavicle check x-ray demonstrating an apical pneumothorax and an excessively long medial screw (white arrow); **Figure 1b** (bottom) demonstrating a left-sided pneumothorax (white arrow pointing to edge of lung).

Fractures of the clavicle are common representing 2.6 to 5% of all fractures and approximately 80% of fractures affect the middle third of the clavicle.[1] The incidence of high-energy fractures with displacement, comminution and shortening is increasing and as a result operative fixation for such injuries is being performed more commonly.[1] Infection, implant failure, non-union, scar-related pain, prominent hardware and refracture are the most commonly reported operative complications.[2]

Plate fixation is the most common method of operative management.[3] The plate is most commonly placed on the superior surface of the clavicle with screws inserted in a cranial-caudal direction potentially placing the lung apex and the neurovascular structures at risk during drilling and screw insertion. The risk however of either an iatrogenic pneumothorax or neurovascular injury is regarded in the literature as a rare occurrence.[3,4] Some centres have recommended obtaining a chest x-ray routinely to exclude pneumothorax following clavicle fixation. Shubert et al.[3] concluded from their study that due to the rarity of iatrogenic pneumothorax, radiation exposure and cost, in combination with the poor sensitivity of chest radiographs to detect pneumothoraces, obtaining a routine chest x-ray without clinical indication may be unnecessary.

Pneumothorax in relation to clavicular fractures is a well-described preoperative complication existing in the literature.[3,5] In our case, the patient had a preoperative chest x-ray which did not demonstrate pulmonary trauma and given the excessive difference in length between the most medial screw and the adjacent screw we conclude that the patient incurred an iatrogenic pneumothorax due to surgical error. We acknowledge that intra-operative screening would have identified the long medial screw but the pneumothorax may not have been appreciated.

We emphasise the importance of careful surgical technique when performing plate fixation of a midshaft clavicular fracture, in particular, ensuring a guard is placed under the clavicle when drilling and close attention to screw length. Furthermore, we recommend careful scrutiny of postoperative clavicle radiographs due to the rare but potential risk of iatrogenic pneumothorax.

Miss Rebecca Waterworth

Mr Neville W Thompson

Department of Trauma and Orthopaedics, Altnagelvin Hospital, Glenshane Road, Londonderry BT47 6SB

Correspondence to: Mr Neville W Thompson, Consultant Trauma and Orthopaedic Surgeon, Altnagelvin Hospital, Glenshane Road, Londonderry BT47 6SB

Email: neville.thompson@westerntrust.hscni.net

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BRASH SYNDROME: AN UNDER RECOGNISED CAUSE OF COMPLETE HEART BLOCK IN THE ELDERLY

Editor,

An 81 year old lady with a background of chronic kidney disease (CKD), hypertension and type two diabetes mellitus presented to Craigavon Area Hospital via ambulance as a stroke lysis call. She was dysarthric and profoundly bradycardic with an unreadable blood pressure. Following administration of 600mcg atropine a blood pressure of 100/60mmHg was obtained. An ECG demonstrated complete heart block (CHB) with a ventricular rate of 29 bpm (Figure 1). A further 1.8mg atropine did not rectify her CHB and ventricular rate remained 40bpm albeit with a satisfactory blood pressure. Dysarthria was felt to be secondary to cerebral hypoperfusion in the context of CHB and her management was deferred to the cardiology team with the assumption that she would require a pacemaker.

An arterial gas sample was taken at this point which demonstrated elevated potassium of 8.3mmol/L. Interestingly, her ECG did not demonstrate dramatically peaked T waves as would be expected with hyperkalaemia and initially this first reading was thought to be erroneous. Repeat sampling

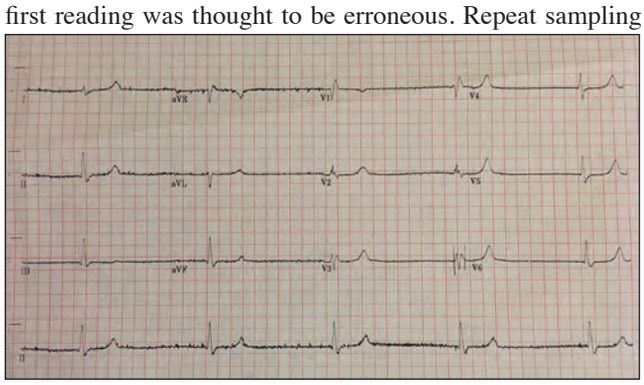

Figure 1 ECG demonstrating ventricular escape rhythm 29bpm without discernible atrial activity. RSR pattern with QRS 140bpm in keeping with RBBB noted in v1-3 with QRS in remaining leads noted to be relatively narrow with mild peaking of T waves noted.

however confirmed hyperkalaemia. Additionally, her formal laboratory biochemistry soon confirmed she was in acute on chronic renal failure with an eGFR of 12mls/min which had deteriorated from a baseline of 30mls/min. The hyperkalaemia remained refractory to conventional medical treatment and haemofiltration was commenced. Upon normalisation of serum potassium, her rhythm reverted to sinus of rate 74bpm (Figure 2). Haemofiltration was weaned over the coming days and a permanent pacemaker was not required.

It emerged she had been taking both atenolol and Ramipril for hypertension and had recently commenced a NSAID for joint pain. This likely precipitated an acute nephrogenic

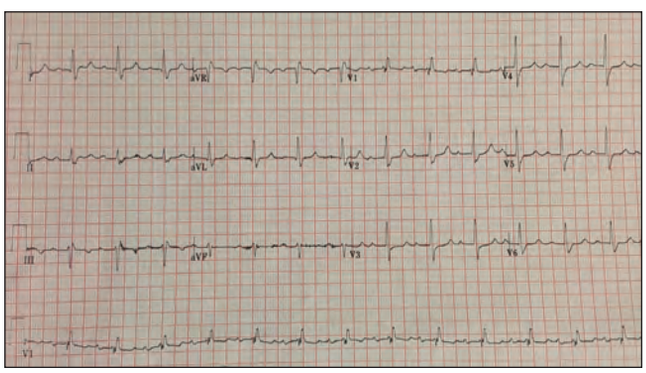

Figure 2 ECG demonstrating restoration of Sinus rhythm with mildly prolonged PR interval of 240ms.

insult resulting in the accumulation of atenolol causing further renal hypoperfusion and hyperkalaemia which, in synergy with B-blockade, precipitated CHB and cerebral hypoperfusion.

This case illustrates the recently coined BRASH syndrome (Bradycardia, Renal failure, AV-node blockers, Shock and Hyperkalaemia). This describes a series of events in a patient with CKD taking AV nodal blockers where an initial insult (such as dehydration or nephrotoxic medication) triggers a cascade of events where AV nodal suppression impairs the normal compensatory response to renal hypoperfusion thus causing renal decompensation resulting in worsening hyperkalaemia. The synergistic effect of hyperkalaemia and B-blockade on AV nodal function causes further decompensation resulting in a pathological downward spiral of events.[1,2]

This is an under-recognised cause of CHB and renal failure which may be refractory to initial conventional treatment measures. ECG changes may not be characteristic of classical hyperkalaemia, occur at lower than expected serum potassium levels and remain refractory to conventional treatment.[3,4] Co-morbid elderly patients on multiple medications are at high risk of developing this syndrome therefore as physicians we must be cognisant of prescribing AV nodal blockers or indeed additional nephrotoxic agents, so as to not incite the pathological cascade of events leading to BRASH syndrome.

Patrick Savage[1] David McEneaney[2]

Correspondence to: Dr Patrick Savage.
E-mail: psavage05@qub.ac.uk

1). Specialty Registrar in Cardiology - Craigavon Area Hospital, Southern Health and Social Care trust.

2). Consultant Cardiologist - Craigavon Area Hospital, Southern Health and Social Care trust.

Keywords: *BRASH Syndrome, Hyperkalaemia, complete heart block, pacing, polypharmacy, elderly care medicine, cardiology, nephrology*

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DEGLUTITION SYNCOPE – A CASE REPORT

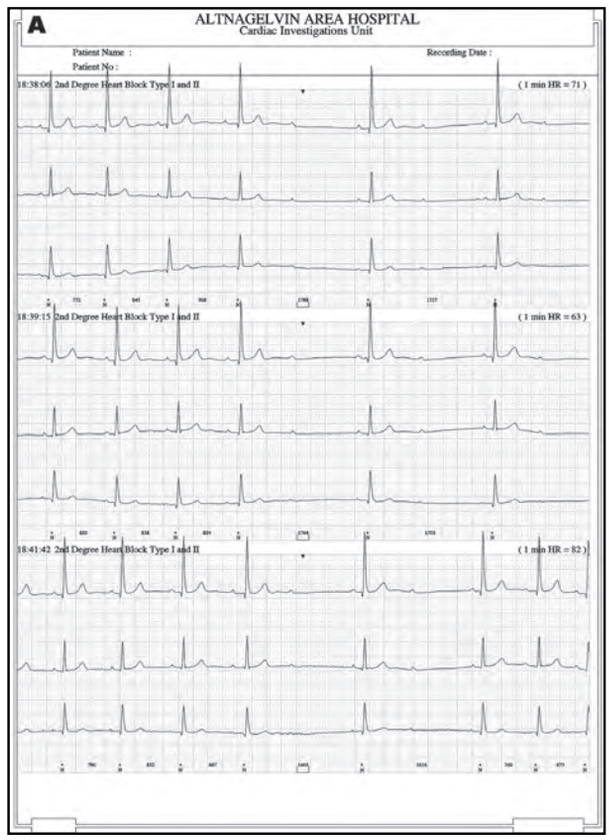
Editor,

A 38-year-old woman was referred to hospital for investigation following a three-year history of lightheadedness, dizziness and poor balance associated with eating. During this period, she had one episode of loss of consciousness. Symptoms were associated with flushing of the face which resolved spontaneously within 15 seconds. She reported that she could have up to fifteen episodes per week. She denied headaches and did not have any autonomic problems with her bladder or bowels. She had no significant past medical history. She did not take any regular medication and had no known allergies.

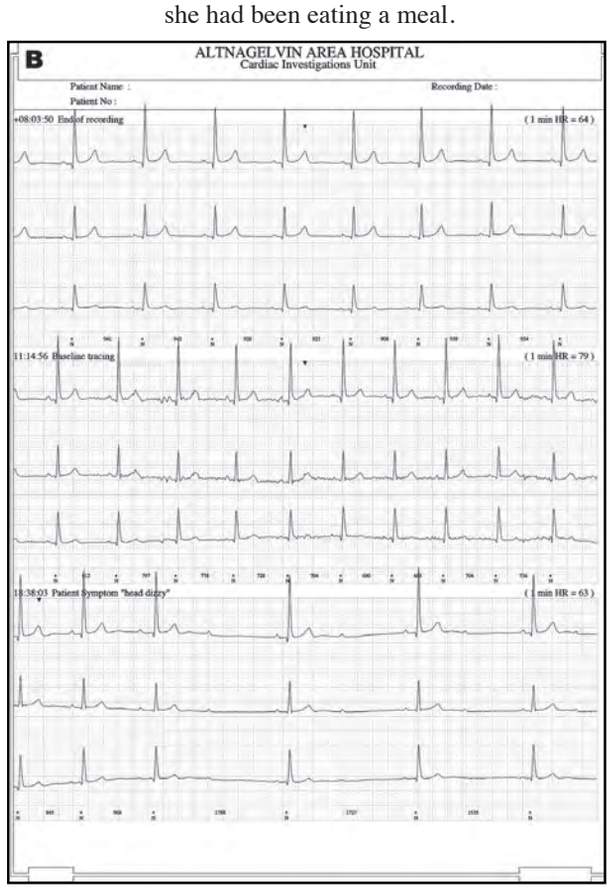
Blood pressure and heart rate were within normal ranges and she had no postural hypotension. A 12-lead ECG showed normal sinus rhythm with QTc interval within normal limits at 400ms.MRI brain and EEG were unremarkable. A 24-hour ambulatory ECG showed episodes of Mobitz Type 2 second degree atrioventricular block of which the patient was symptomatic, all occurring whilst she was eating (Figure 1 (a) and (b)). A diagnosis of swallow or deglutition syncope was made. Permanent pacemaker was implanted with complete resolution of symptoms.

DISCUSSION

Swallow syncope is a rare disorder thought to be due to a vagus nerve-mediated reflex. An increase in afferent



Figures 1 (a) and **(b)** showing 2nd degree heart block. On both occasions, the patient had documented that she had been eating a meal.



vagal activity from the oesophageal plexus to the nucleus solitarius in the medulla is associated with swallowing food. Efferent parasympathetic fibres to trigger peristalsis have a cardioinhibitory effect and lead to bradycardia, hypotension and vasodilatation. Severe cardiac conduction disturbance may cause loss of consciousness [1]. Over one hundred cases have been described in literature[2], despite having been first reported[3] in 1793.

The management of swallow syncope should include the withdrawal of any medication that slows the rate of cardiac conduction or causes vasodepression. Anticholinergic medications such as atropine have been trialed with a view to prevent bradyarrhythmias by inhibiting vagal tone. However, results have been inconsistent, and many drugs have undesirable side effects and are therefore poorly tolerated [2] .

Eighty-five percent of reported cases of swallow syncope had either sinus bradycardia, sinus arrest, SA block or AV block. Implantation of a permanent pacemaker is increasingly used for patients with swallow syncope [4]. Whilst permanent pacemaker implantation does not correct the cause of the condition, it has been demonstrated to be an effective treatment.

Dr. Ciara O'Hare MBChB
Dr. Mark McCarron FRCP
Dr. Paul McGlinchey FRCP
Dr. Divyesh Sharma FRCP

Cardiac Unit
Altnagelvin Area Hospital
Londonderry
BT47 6SB

Corresponding author
Dr. Divyesh Sharma MSc, FRCP, FESC

E-mail: Divyesh.Sharma@westerntrust.hscni.net

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FOLLICULAR LYMPHOMA OF THE RECTUM

Editor,

Non-Hodgkin's lymphoma compromises a diverse group of malignant neoplasms, rarely involving the colorectum. [1, 2] Follicular lymphoma is a common subtype and constitutes 1%–3% of all primary gastrointestinal tract lymphomas. [1, 3] There are very few cases reported of recurrence of follicular lymphoma in the rectum. [4] Rectal follicular lymphoma is difficult to diagnose due to limited available data, low clinical suspicion and non-specific symptoms. It also has variable growth pattern and ill-defined histopathological picture, making it difficult to distinguish from benign proliferative lymphoid lesions. [3]

This 67-year-old lady presented in January 2010 with a right neck mass. Initially she was managed with watchful waiting for putative atypical lymphoproliferative disorder, but in August 2011 histopathology confirmed follicular non-Hodgkin's lymphoma which was treated successfully with chemotherapy. In May 2016 she presented with worsening faecal incontinence and a palpable rectal mass. Clinically,

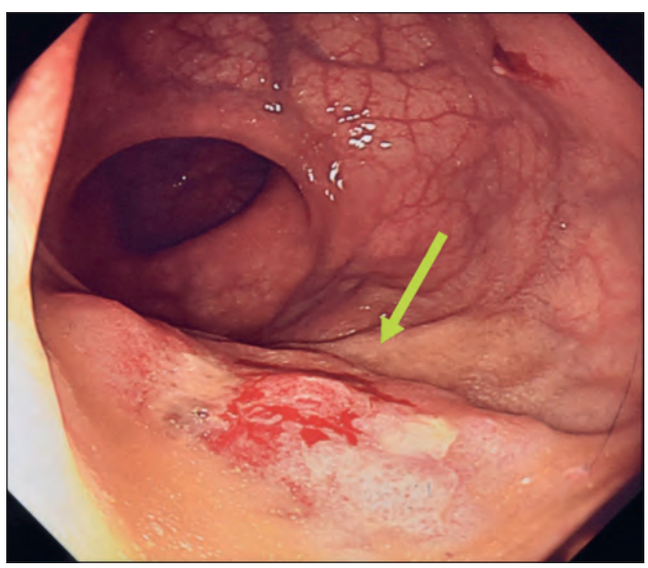

Figure 1 - Endoscopic appearance of low rectal lesion (arrowed)

this appeared to be a low rectal adenocarcinoma. [Figure 1 – Endoscopic appearance of low rectal lesion (arrowed)]. Magnetic resonance imaging (MRI) and computed tomography (CT) confirmed this rectal tumour extending to the anorectal junction with a radiological staging offered at – T3N1Mx. [Figure 2 – MRI view (coronal) demonstrating the low rectal lesion]. The initial biopsy showed a probable high-grade lymphoma, but two subsequent biopsies demonstrated only chronic inflammation. Another biopsy in December 2016 confirmed the presence of a low-grade follicular lymphoma. The patient was clinically stable and given the locality of the disease and the significant risks of chemo/radiotherapy a 'watch and wait' approach was chosen. However, her symptoms progressed and in January 2018 she had low-dose radiotherapy in the pelvis. As of September 2018, the patient has had a relapse confirmed and is under the ongoing care of haematology/oncology.

Gastrointestinal tract follicular lymphomas have usually inert clinical course. Patients can present with various non-

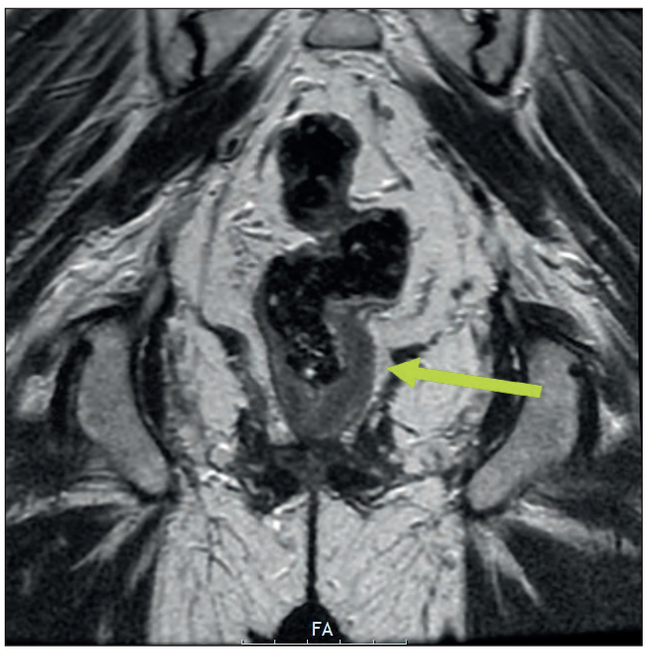

Figure 2 - MRI view (coronal) demonstrating the low rectal lesion

specific symptoms, but faecal incontinence has not been previously reported in the literature.[1 2 5] The histopathological evaluation of colorectal follicular lymphoma can be difficult. It is not uncommon for initial histological misinterpretation and requirement of multiple biopsies before the definite diagnosis. This case emphasises the challenge of accurate histopathological diagnosis. Suitable biopsy samples and immunophenotyping analysis are recommended for accurate interpretation of the pathological diagnosis of follicular lymphoma.[4, 5] The management of gastrointestinal follicular lymphoma is not well established because of its rarity, but multidisciplinary approach should be undertaken. In this patient, after a watchful period, local radiotherapy was implemented with good effect. This appears in accordance to general consensus, as intestinal follicular lymphoma is usually approached as nodal follicular lymphoma and a watch-and-wait strategy or radiation therapy can be applied in case of limited disease.[1]

In conclusion, rectal follicular lymphoma is a rare presentation, but important to consider in the differential diagnosis of rectal lesions. Endoscopists should remain alert whenever they observe ambiguous lesions in the colorectum and consultation with pathologist is advised to ensure appropriate immunostaining. Histopathologists should also maintain high clinical suspicion in differential diagnosis of follicular hyperplasia of mucosa-associated lymphoid tissue.

***Sevasti Konstantinidou MRCS** Core trainee in Surgery

Charlotte Cosgrove MRCS Registrar in Surgery

William Campbell BSc PhD FRCSI Consultant Colorectal Surgeon

Department of Colorectal Surgery, Causeway Hospital, 4 Newbridge Road, Coleraine, UK

***Corresponding author** – sevastgk@hotmail.com

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TACKLING ANTIMICROBIAL RESISTANCE (AMR) - IN VITRO EFFECT OF SODIUM CHLORIDE ON ANTIBIOTIC SUSCEPTIBILITY IN CLINICAL PSEUDOMONAS AERUGINOSA ISOLATED FROM PATIENTS WITH CYSTIC FIBROSIS (CF)

Editor,

Relatively little is known about the potential interactions of cystic fibrosis (CF) co-therapies on antimicrobial susceptibility in CF respiratory pathogens, particularly inhaled/nebulised interventions, including those aiding sputum clearance, in particular, hypertonic saline (HTS). Whilst such interventions are not designed *per se* as anti-infectives, the effect (if any) of such molecules to CF patients' microbiological status and the potential effect on antibiotic susceptibility merits careful monitoring. Hence, we examined the effect of hypertonic saline on the *in vitro* antibiotic susceptibility to clinical *P. aeruginosa* from adult CF patients.

P. aeruginosa isolates (n=50) from adult CF patients were examined and were obtained from freshly expectorated sputum specimens submitted by adult CF patients, as part of the routine microbiological workup. Antibiotic susceptibility of each isolate was assessed employing standard CLSI disk diffusion assay,[1] against the antibiotics listed in Table 1, in the presence of sodium chloride (0.6M) and without supplementation, where 0.6M NaCl was chosen as a surrogate for NaCl concentration in sputum following HTS treatment. Resulting zone of inhibition were measured (mm) and compared statistically employing a two-tailed paired t-test, where p values <0.05 were considered significant, as shown (Table 1).

There was a significant effect on antibiotic susceptibility when supplemented with NaCl (0.6M). For each class of antibiotic examined, there was a statistically significant increase in zone size, ranging from a 19.3% increase with tobramycin to an 81.8% increase for piperacillin/tazobactam, with a mean increase of 60.1% over all classes of antibiotics examined.

Table 1: *In vitro effect of supplementation with sodium chloride (0.*6M) on antibiotic susceptibility of clinical isolates of *Pseudomonas aeruginosa* isolated from the sputum of patients with cystic fibrosis

	Mean Zone size (mm)			
Name of antibiotic	**Antibiotic alone**	**Antibiotic + 0.6M NaCl**	**Change in zone size (%)**	**P value**
Piperacillin/Tazobactam	20.9	38.0	+81.8	<0.0001
Meropenem	23.6	39.5	+67.4	<0.0001
Tobramycin	15.0	17.9	+19.2	0.02
Ciprofloxacin	17.3	30.0	+73.4	<0.0001
Colistin	13.7	21.7	+58.4	<0.0001

Using CLSI interpretative criteria, these changes in mean zone size would shift intermediate resistant isolates for piperacillin-tazobactam and ciprofloxacin to being sensitive, with the others remaining sensitive, with and without salt supplementation, albeit with increased susceptibilities in the presence of salt.

The mechanisms contributing to enhanced antibiotic susceptibility in the presence of increased saline concentration (0.6M) are not fully understood, but it appears that increased osmotic pressure is responsible for altered MIC value. *P. aeruginosa* cells had been precultured in isotonic conditions and were suddenly exposed to unusual hypertonic conditions, leading to a sudden change in external osmotic pressure. The immediate result of this would have been water efflux and cell dehydration, leading to adversely altered cytoplasmic solute concentration and a disruption in normal cellular physiology. Additionally, such osmotic stress would lead to alterations in physical properties of the cell architecture, including cell volume of the cytoplasm/periplasm, turgor pressure, cell wall strain and cytoplasmic membrane tension.[2]

The increasing burden of AMR amongst CF bacterial pathogens is clinically important, as it limits the efficacy of antibiotics used. Therefore, any positive shift in regaining susceptibility is to be welcomed and exploited, to maintain the effectiveness and value of the current CF antibiotic formulary.

In conclusion, the inclusion of NaCl demonstrated an increase in zone diameters for all antibiotics tested. Our results suggest a potential synergistic effect of NaCl and commonly used anti-pseudomonal antibiotics. Further work is now needed to evaluate the *in vivo* effect of HTS and PA antimicrobial therapy and if the reduced MIC is maintained over time.

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DECLARATION OF INTERESTS

The authors have no interests to declare.

Andrea Gramegna[1,2,3*], B. Cherie Millar[1,2,5], M. Contarini[3], Francesco Blasi[3], J. Stuart Elborn[4,6], Damian G. Downey[2,4] and John E. Moore[1,2,4,5*]

[1] Department of Bacteriology, Belfast City Hospital, Belfast Health & Social Care Trust, Lisburn Road, BELFAST, BT9 7AD, Northern Ireland,

[2] Regional Adult Cystic Fibrosis Centre, Belfast City Hospital, Belfast Health & Social Care Trust, Lisburn Road, BELFAST, BT9 7AD Northern Ireland,

[3] Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Internal Medicine Department, Respiratory Unit and Regional Adult Cystic Fibrosis Center, IRCCS Fondazione Cà Granda Ospedale Maggiore Policlinico, Milan, Italy

[4] Centre for Experimental Medicine, Queen's University Belfast, Northern Ireland,

[5] School of Biomedical Sciences, Ulster University, Cromore Road, Coleraine, BT52 1SA, Northern Ireland.

[6] Imperial College and Royal Brompton Hospital, London

Corresponding author: Professor John E. Moore,

E-mail: jemoore@niphl.dnet.co.uk

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FIRST CASE OF COVID-19 IN IRELAND

Editor.

Covid-19 is the disease caused by SARS-CoV-2 virus[1]. Some notable members of this family include MERS-CoV and SARS-CoV which were responsible for epidemics in the past[1]. On 11th March 2020, WHO declared Covid-19 to be a pandemic and urged the world to come together in order to slow down further spread of this virus[2].

We present the first case of Covid-19 diagnosed in Ireland. This middle-aged lady travelled to Northern Italy and returned on 17th February 2020. On the same day, she developed general malaise and cough. Symptoms persisted and she developed dyspnoea and fever which prompted her to seek advice from her GP.

Following advice from the Public Health Agency, samples were taken, and on the 26th February, SARS-Cornavirus -2 RNA was detected in a Nasal and Throat Swab (NTS) using previously published real-time PCR assays[3]. Briefly, the screening assay targeted the RNA dependent RNA polymerase (RdRP) gene, with positivity confirmed using assays targeting the envelope (E) and nucleocapsid (N) genes. RNA was extracted with the MagNAPure Compact system (Roche, UK) and real-time PCR for each gene target run as a 25ul reaction (containing 5ul RNA, 12.5ul of 2X Superscript III of step RT-PCR reaction buffer, 0.4uM dNTPs, 3.2mM $MgSO_4$, 1ul of RT/Taq enzyme (Invitrogen, UK) and primer and probe concentrations for the respective assays. PCR cycling conditions using LightCycler 480 II were as follows: 55 °C for 10 min for reverse transcription, 95 °C for 3 min and 45 cycles of 95 °C for 15 s, 58 °C for 30 s. Ct values less than 40 were reported as positive.

On the 27th February, the patient was admitted for clinical observation and containment. She reported the following symptoms during her stay: cough, night sweats, fever, nausea, loose BO, dyspnoea, chest pain, nausea, general malaise and headache. Her vital signs showed low grade pyrexia with a maximum temperature of 38°C. The lowest peripheral oxygen saturation was 92% (on room air). She remained haemodymically stable throughout her stay. Blood investigation showed mild leucopenia at $3.5x10^9$cells/L, lymphopenia at $0.9x10^9$ cells/L, and maximum CRP was 27 mg/L. X-ray demonstrated no evidence of pneumonia. The NTS remained positive until last sampled on the 11/3/2020 (i.e. at least 15 days' duration). She suffered ongoing dyspnoea on minimal exertion. Investigations including D-Dimer, Cardiac Troponin, ECG and CXR demonstrated no acute abnormality.

This lady had a mild clinical episode of Covid-19. Young et al reports prolonged viral shedding in nasopharyngeal samples up to 24 days[4]. As this pandemic unfolds, admission will be reserved for confirmed and suspected cases with symptoms and signs of severe disease.

Written informed consent was obtained from the patient for publication of this case report.

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No conflict of interest to declare.

Dr Vi Perumal, Dr T Curran, Dr M Hunter.

Department of Infectious Diseases

East Wing, Royal Victoria Hospital, Belfast.

Correspondence to: Dr Michael Hunter.
E-mail: Michael.Hunter@belfasttrust.hscni.net

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MYELOLIPOMA IN THE KIDNEY TRANSPLANT: A UNIQUE ENTITY TO BE ACKNOWLEDGED

Editor,

Kidney transplantation is the best treatment option for end stage renal disease and the impact of cancer affecting the transplanted graft is higher when compared to the general population. It significantly affects the patient quality of life, meaning return to dialysis, along with worse life expectancy[1]. It is therefore envisaged to be able to discern between benign lesion treatable conservatively or with surveillance and those requiring graft nephrectomy[2]. In particular, misdiagnosis of rare entities such as myelolipoma, could represent a challenge requiring dedicate expertise.

Myelolipoma is often incidentally discovered, with no laboratory alterations. Less than 10 cases have been reported in the native kidney as well as in the surrounding tissue[3]. There is no association with gender and tends to be more common in the seventh decade of life, with the first case described in 1905 by Gierke in the adrenal[4], its preferential site. On imaging, it tends to show as a solid mass with fat density attenuation and no contrast-enhancement.

At our Institution, we have treated the only myelolipoma involving a transplanted kidney. This was in a 48 years old male with persistent high C-reactive protein levels,

despite no infection source identifiable. His past medical history included Bardet–Biedl syndrome, blindness and kidney failure secondary to reflux nephropathy, for which he underwent deceased donor kidney transplantation 20 years before that worked for 18 years. The failed transplant was left in situ for the remaining two years, on immunosuppression consisting of cyclosporine and prednisolone. At this time, he experienced repeated hospital admission with raised inflammatory markers and fever. On imaging concerns were raised about liposarcoma around his left sided renal transplant (Figure 1). Decision was made to proceed with graft nephrectomy and excision of the retroperitoneal mass

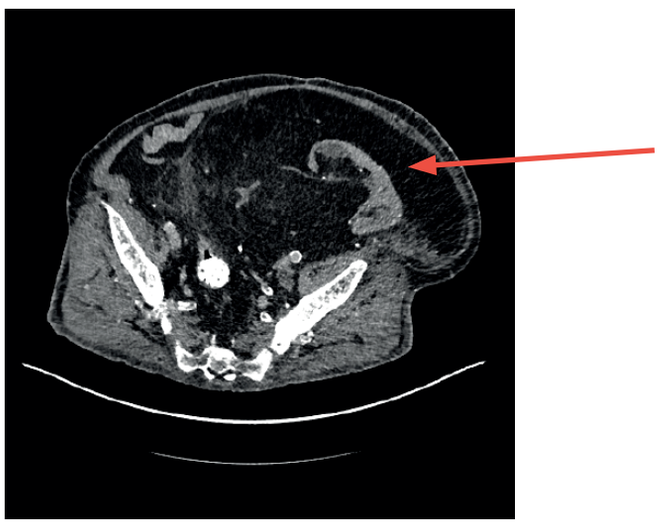

Figure 1 - Suspected malignant lesion surrounding the left sided kidney transplant (arrow)

(Figure 2). The operation required also ileofemoral arterial bypass and ileofemoral venous bypass in order to achieve radical oncology. Post-operative course was characterised by deep vein thrombosis, for which he was therapeutically treated with enoxaparin. The patient was discharged on 12 days after surgery, with current follow up of 1 month.

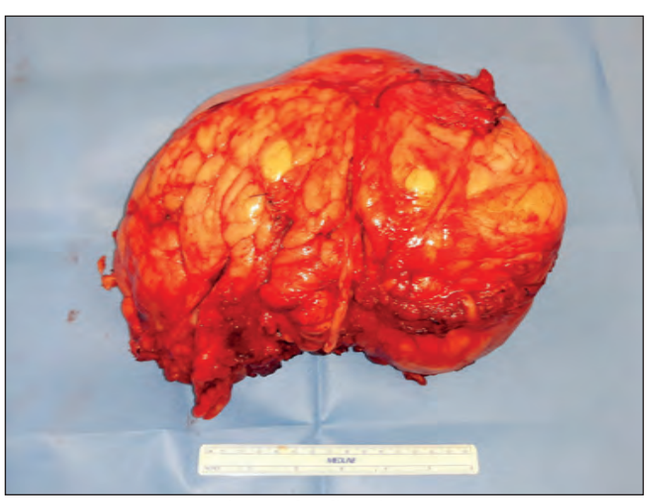

Figure 2 - Specimen.

In view of this unicity, the majority of clinicians would be unfamiliar with the features and management of myelolipoma in the kidney graft, and indeed even our first diagnosis was of a malignant lesion leading us to pursue a more aggressive treatment, with major vascular reconstruction. The patient was already on dialysis, but more debate regarding the most effective treatment would rise for working grafts. Retrospectively, more awareness of this rare disease, with attention to its radiological features and consideration of risk factors such as endocrine (Bardet–Biedl syndrome) and hematopoietic disorders (long effects of immunosuppression) might have been considered and possibly modified the intended radical oncology.

In conclusion, treatment options of rare benign diseases such as myelolipoma have to be tailored to patient needs, with a conservative management preferable for small, asymptomatic lesions or working grafts and partial/radical nephrectomy in enlarging masses. Embolization is rarely effective, as often the only vascularity present is small and peripheral.

Maria Irene Bellini1, Hanna Magowan1, Oisin Houghton[2], Julie Reid[3], James McDaid[1]
[1]Regional Transplant Unit, Belfast City Hospital, Belfast BT9 7AB, UK.
[2]Department of Histopathology, Belfast City Hospital, Belfast BT9 7AB, UK.
[3]Vascular Surgery Department, Royal Victoria Hospital, Belfast BT12 6BA, UK.
Corresponding author: Maria Irene Bellini, Belfast City Hospital, Belfast Health and Social Care Trust, 51 Lisburn Road, Belfast, United Kingdom BT97AB
Phone: +44 0 2896156671
E-mail: m.irene.bellini@gmail.com
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THE MICROBIOLOGY OF THE *CAMÁN*

Editor,

Camogie is a popular sport amongst women and involves an estimated 100,000 players, administrators, referees and coaches through 573 clubs across Ireland, as well as clubs in Europe, Australia and North America (www.camogie.ie). Fifteen-a-side camogie is a stickhandling, high velocity, multidirectional field sport,[1] played with a hurl or *camán*, which is usually crafted from ash (*Fraxinus excelsior*) plants. The hurl is not allowed to be greater than 13cm in width at its base, thus combined with the high velocity nature of the game, sports injuries in camogie have been reported, which have mainly consisted of hand, facial and laceration injuries.[2] Given the history and potential for lacerations and open wounds from hurl-related injuries, we wished to examine the microbiological flora of these, with particular attention to the types of bacteria that may be potentially introduced from the hurl into an open wound, from a laceration-related injury.

Hurls (n=24) were sampled anonymously from active amateur camogie players in the Ulster provincial game during active training sessions. A 2cm x 2cm area of each hurl was swabbed using a sterile pre-moistened transport swab (Sterilin, UK) and was examined microbiologically by inoculating the swab onto Standard Plate Count agar (Oxoid CM0463, Basingstoke, UK), followed by incubation at 37°C for 48h, as previously described.[3] Resulting colonies, which were phenotypical different, were purified and identified using matrix-assisted laser desorption/ionization – time-of-flight (MALDI-TOF) mass spectrometry technology. The taxonomy of bacteria identified is shown in Table 1.

Seven bacterial species were identified from the surface of the hurls, including four Gram-positive bacteria and three Gram-negative bacteria, from six taxonomic genera. The natural niche of these bacteria is the environment, including soil, so it is most likley that the wooden hurls became contaminated when they were in contact with the soil on the grass pitch. Whilst some of the bacterial species isolated have previously shown some degree of pathogenecity in infection and therefore may be considered as opportunistic pathogens, they are not normally considered to be an infection risk to immunocompetent hosts, such as healthy camogie players.

Laceration injuries in camogie which are inflicted from a hurl should seek medical advice and appropriate wound management. GPs and Accident & Emergency clinicians should be aware of the spectrum of endogenous organisms from the player's skin, as well as those detailed above originating from the hurl, in any related wound complication from such injuries. Additionally, whilst our study did not isolate any *Clostridium tetani* organisms, given the origin of the organisms we identified as being from soil, camogie players should ensure that they are have a complete and up-to-date tetanus vaccination record and should seek re-vaccination in accordance with the Green Book,[4] where there is an incomplete vaccination history or where defecits exist.

John E. Moore[1,2*], John McCaughan[3], Mollie Maguire[2] and B. Cherie Millar[1,2]

[1] Northern Ireland Public Health Laboratory, Department of Bacteriology,
Nightingale (Belfast City) Hospital, Lisburn Road, Belfast, Northern Ireland, BT9 7AD,

[2] School of Medicine, Dentistry and Biomedical Science, The Wellcome-Wolfson Institute for Experimental Medicine, Queen's University, 97 Lisburn Road, Belfast BT9 7BL, Northern Ireland,

[3] Department of Medical Microbiology, Royal Group of Hospitals, Grosvenor Road, Belfast, BT12 6BA, Northern Ireland.

***corresponding author**
Professor John E. Moore,
Northern Ireland Public Health Laboratory,
Department of Bacteriology,
Belfast City Hospital,
Belfast, BT9 7AD,
Northern Ireland,
United Kingdom.
Tel: +44 (28) 9026 3554
Fax: +44 (28) 9026 3991
E-mail: j.moore@qub.ac.uk
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DEATH FROM DIABETES IN IRELAND/HISTORY

Editor,

In your journal in 1987 Crawford reported on the history of deaths from diabetes in Ireland.[1] His report showed that in the second half of the nineteenth century death rates associated with diabetes rose exponentially and he hypothesized that this was due to increases in the intake of carbohydrate and fat. For the last thirty years I have always opened my lectures on type 2 diabetes with this report. However, due to recent information from epidemiological studies of the consequences of famines, I believe that the original interpretation of this study is incorrect.

China's Great Famine (1959-1961) showed that adults born between 1960 and 1961 had a 23% increased risk of developing diabetes and if born in a particularly affected area

there was a 40% increase. This suggests that fetal exposure during the famine increased the risk of diabetes in adulthood.[2]

In the Ukraine Famine, individuals born between 1930 and 1939 had in 2001 an increased risk of developing diabetes. The prevalence of diabetes increased by 47% in those born in regions with severe famine compared with those born in areas where a famine did not occur.[3]

The Dutch Winter Famine occurred during the final six months of the second World War. 702 subjects born in Amsterdam between November 1, 1943 and February 20, 1947 were shown at age 50 to be more likely to have glucose intolerance and insulin resistance.[4]

The Irish Potato Famine began in 1845 and ended in 1852. From Crawford's paper it can be seen that the greatest increase in death from diabetes occurred between 1880 and 1911 when those born during the famine would be between 30 and 60 years old.

The reason that starvation in utero is associated with a higher risk of type 2 diabetes in later life is that the fetus prepares for its likely adult environment which is not encountered (thrifty phenotype). These epigenetic changes are due to increased gene activity and expression rather than by starvation induced changes in the DNA sequence.[5]

Therefore, after 33 years, I believe it is time to reinterpret Crawford's data and conclude that the large increases in death from diabetes during nineteenth century in Ireland was due to the in utero effects of starvation during the Irish Potato Famine and not due to increases in the intake of fat and sugar.

The author has no conflicts of interest.

David S. H. Bell, Professor Medicine (retired)
University of Alabama Medical School
1900 Crestwood Blvd, Suite 201
Irondale, AL 35210
Correspondence to David Bell, MB

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SEPTIC CAVERNOUS SINUS THROMBOSIS; A RARE CAUSE OF UNILATERAL EXOPHTHALMOS

Editor

We wish to present an interesting case of Septic Cavernous sinus thrombosis (CST), which is fatal yet infrequent condition associated with high mortality and debilitating morbidity.[1] A 28-year-old man presented with cold like symptoms for 7 days which progressed into worsening headache, fever and nausea. His past medical history was unremarkable with no recent travel history. His examination revealed temperature of 38.1 ^{0}C and facial puffiness with no other systemic findings. His investigations only showed raised C-reactive protein 288 mg/L and white cell count 15.0 x 10^{9}/L. In light of headache and visual symptoms he had Computerized tomography scan (CT) Head done without contrast which only revealed sphenoid & posterior ethmoid sinusitis. He remained febrile for four days despite being on broad spectrum antibiotics, and on day 5 he developed double vision, Cranial nerve VI palsy and unilateral exophthalmos, confirmed by formal ophthalmological/orthoptic assessment with no papilledema or any retinal disease. Repeat CT imaging of head/orbits failed to identify any cause of unilateral exophthalmos. Both initial blood cultures from the admission of day grew Proteus mirabilis sensitive to pipercillin/tazobactam while subsequent multiple blood cultures did not grew any organisms. A CT Head venogram was performed which confirmed a filling defect consistent with CST and inflammatory changes in sphenoid & ethmoid sinuses (figure 1 and 2). Other investigations such as chest X-ray, viral serology, abdominal ultrasound, echocardiogram, lumbar puncture, urine and stool cultures were all negative for any alternate source of infection.

He was initially treated with ceftriaxone/amoxicillin for

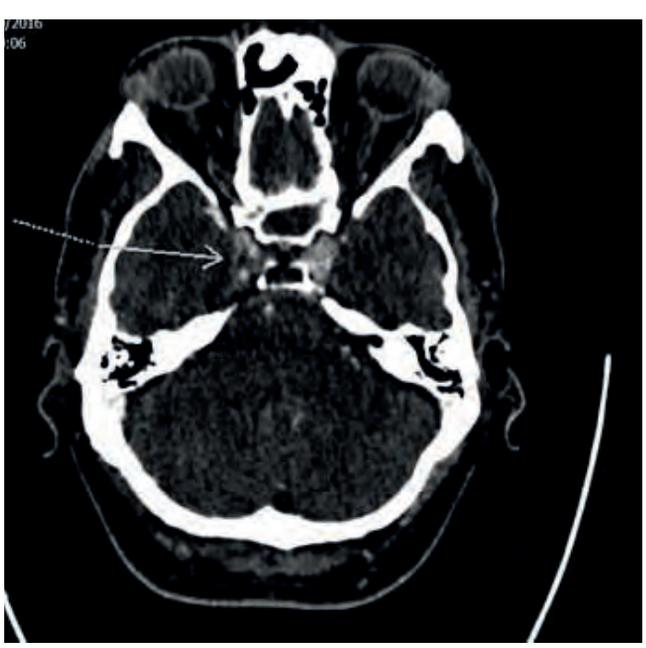

Figure 1 CT Venogram with arrow showing the cavernous sinus thrombosis on the right

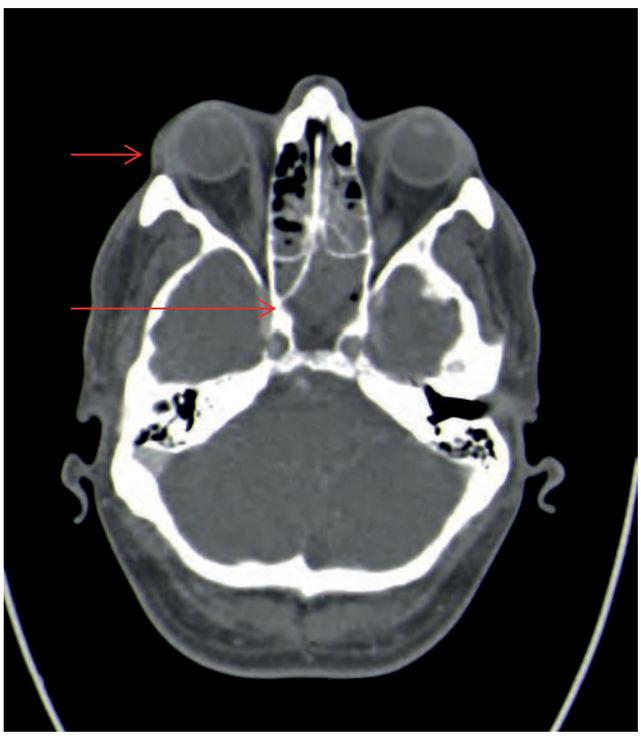

Figure 2 CT Venogram showing exophthalmos on the right (short arrow) and sphenoid sinusitis (long arrow)

3 days for possible meningitis which was later switched to piperacillin/tazobactam as per sensitivity on the blood cultures. After no response clinically and confirmation of septic CST, he was started on therapeutic dose of low molecular weight heparin alongside intravenous Meropenem and Metronidazole (combination therapy) on day 6, to effectively cover a wide number of potential organisms including Proteus mirabilis. He underwent urgent functional endoscopic sinus surgery (FESS) and stopped spiking temperature 24 hours later. Nasal swab culture during FESS grew mixed faecal flora of indeterminate significance. He was discharged home on day 16 to complete antibiotics and anticoagulation for another 4 weeks. On review after 8 weeks he had complete resolution of his symptoms with normal MRI venogram.

CST of septic origin is associated with significantly high mortality (23%) despite advances in medical care.[2] Retrospective studies on anticoagulation in septic CST have shown some benefit in reducing mortality and morbidity such as blindness, opthalmoplegia, seizures and stroke; hence experts suggest anticoagulation for a minimum of 4 weeks.[3]

The authors' main purpose of this letter is to raise awareness around diagnosis of this condition as septic CST can only be identified with high index of suspicion, requires early imaging with correct modality (either CT or MRI Venogram) and prompt initiation of antibiotics as well as surgical intervention and potential anticoagulation, all of which are paramount to preventing long-term complications and mortality.

Authors
Adnan Agha[1*]
Terence Pang[2]
Oluwasola Ajayi[3]
Alexandra Lubina Solomon[2]

1. Consultant Department of Acute Medicine University Hospitals of Derby and Burton NHS
2. Consultant Department of Diabetes & Endocrinology, Russells Hall hospital, Dudley Group NHS Foundation Trust
3. Consultant Department of Diagnostic and Interventional Radiology, Russells Hall hospital, Dudley Group NHS Foundation Trust

***Corresponding author email:** adnanagha@nhs.net

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