

Letters

CHOLECYSTOSTOMY FOR ACALCULOUS CHOLECYSTITIS WITH HAEMOBILIA IN A LUNG TRANSPLANT PATIENT; A CASE REPORT.

Editor,

We report on a 64 year old gentleman who developed an early broncho-pleural fistula following a double lung transplant for end-stage COPD/Bronchiectasis and was transferred to his referring institution for palliative management.

Ten weeks post-transplant, the patient developed sudden-onset severe epigastric/right upper quadrant abdominal pain. He was tachycardic, normotensive, and had a palpable tender mass in the right hypochondriac region. Blood tests revealed an elevated white cell count and an acute derangement of his liver function tests.

Urgent Computed Tomography (CT) scan of chest, abdomen and pelvis showed a distended gallbladder of mixed attenuation with no peri-inflammatory changes as shown in Figure 1. There was no previous history of gallstones and no gallstones were seen in imaging.



Fig 1. CT scan of abdomen demonstrating a distended gallbladder of mixed attenuation with no peri-inflammatory changes

Due to the critically ill nature of the patient, an urgent percutaneous cholecystostomy was undertaken by ultrasound guidance and a pigtail catheter inserted, which drained a mixture of bile and blood. He was empirically treated with Tazocin (Piperacillin and Tazobactam) 4.5g three times a day.

CMV Polymerase Chain Reaction analysis was positive for both serum and bile and a diagnosis of CMV acalculous

cholecystitis with haemobilia was established. The patient was treated with intravenous ganciclovir for 25 days followed by 18 days of oral valganciclovir. T-Tube cholangiogram 2 weeks following initial insertion demonstrated no flow out of the common bile duct into the duodenum. A Magnetic Resonance Cholangiopancreatography (MRCP) scan (with a view of proceeding to ERCP) demonstrated a normal biliary tree, but showed debris in the gallbladder suggestive of post-haemorrhagic components. A repeat T-tube cholangiogram one week later showed an obstruction at the gallbladder neck. This was managed with two instillations of 25000IU of streptokinase into the cholecystostomy drain 12 hours apart. Repeat T-tube cholangiogram following this demonstrated normal flow of contrast through the common bile duct into the duodenum. The pig tail drain was subsequently removed (day 42) and the patient made a good post-procedure recovery.

CMV infection is common in transplant patients and develops in 3 ways: primary infection (transmission from a seropositive donor allograft to a seronegative recipient), reactivation of latent infection (CMV resembles other members of the herpesviridae in establishing latent infection and so immunodeficiency predisposes to reactivation of CMV) and re-infection (donor-transmitted infection superimposed on reactivation of latent infection).¹ CMV can affect almost any organ system, with infection of the gastrointestinal tract being the most common manifestation of tissue-invasive CMV. It is a rare cause of acalculous cholecystitis in immunocompromised patients with human immunodeficiency virus,² and has been reported in patients following solid organ transplant.³

Ganciclovir remains first-line treatment for CMV disease,⁴ given at a dose of 5mg/kg twice-daily (dose-adjusted for renal impairment). As the drug has no hepatobiliary excretion,⁵ drainage of the gallbladder is mandatory. Treatment duration is patient-specific and should be based on virologic and clinical improvement.

The management of critically ill patients who develop cholecystitis is complex, with percutaneous cholecystostomy an option in the critically ill patient and in patients who are at high risk of general anaesthesia. The procedure allows immediate decompression and drainage of an acutely inflamed gallbladder and can either be used as a temporary bridging measure or as definitive management.

This case is unique in that there are no previous reports of acute CMV cholecystitis developing following lung transplant, and because, as the patient was not fit for cholecystectomy, he was managed with percutaneous cholecystostomy. This case emphasises the usefulness of percutaneous cholecystostomy in the critically ill patient who is unsuitable for surgery.

The authors have no conflicts of interest

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DIALYSIS RELATED AMYLOID ARTHROPATHY ON ¹⁸FDG PET-CT

Editor,

A 60 year-old male patient with end stage kidney disease secondary to Alport syndrome presented with worsening swelling and pain in both shoulders. He had been on regular



Fig 1. Anteroposterior radiograph of the right shoulder showing erosions affecting the coracoid process, humeral head and acromioclavicular joints. The glenohumeral joint space is preserved with no subchondral cystic change present.

haemodialysis for 20 years, having had two failed renal transplants previously and had renal amyloidosis confirmed on renal biopsy. Radiographs of the shoulders showed evidence of an erosive arthropathy affecting the glenohumeral and acromioclavicular joints without significant degenerative change (Figure 1). In view of advanced renal failure and contraindication to MRI, a PET-CT scan was performed with 18-fluorodeoxyglucose (¹⁸FDG) to assess for amyloid involvement in the shoulders. This demonstrated periarticular radiotracer uptake in both shoulder joints with greater involvement on the left, compatible with bilateral amyloid arthropathy in the shoulder joints (Figure 2).

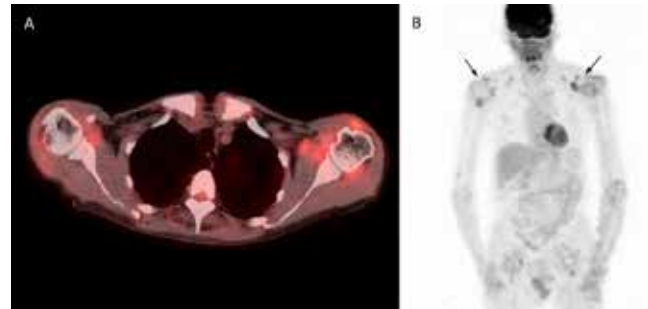


Fig 2. (A) Fused axial ¹⁸FDG-PET/CT image demonstrating periarticular radiotracer uptake in both shoulder joints with greater involvement on the left. (B) Coronal maximum-intensity projection ¹⁸FDG-PET/CT attenuation corrected image demonstrating FDG uptake in the periarticular regions (arrows) consistent with amyloid arthropathy.

Amyloidosis is characterised by extracellular deposition of protein and protein derivatives. The disease becomes clinically significant when its diffuse form affects organ function or when local deposition creates a mass. Our patient had dialysis-related amyloidosis (DRA) which is a well recognized complication in patients on long-term dialysis.^{1,2} Amyloid deposition with β 2-microglobulin has high affinity for collagen and predominantly affects the osteoarticular system.^{3,4} DRA is clinically manifested by an erosive and destructive osteoarthropathy particularly in the form of scapulohumeral periartthritis, carpal tunnel syndrome, bone cysts, spondyloarthropathy and pathologic fractures.¹ As histopathological confirmation is not always possible and because increased serum β 2-microglobulin levels are not diagnostic, the diagnosis is often made by imaging. Diagnosis is essential to prevent more serious complications such as pathologic fractures.

Plain radiography may demonstrate advanced DRA findings such as bone erosions and cystic lesions, but it is not sensitive in the demonstration of early changes and can also underestimate the extent of the disease. Ultrasound can be helpful in the detection of amyloid deposition in the periarticular soft tissues. CT and MRI are useful for the detection of lesions especially in the non-axial skeleton.^{1,3} On MRI, amyloid arthropathy typically demonstrates homogenous low-to-intermediate signal intensity on both T1 and T2-weighted images, and there can be high T2 signal in areas of cystic change. Periarticular amyloid may

enhance mildly after gadolinium administration.^{5,6} However, the administration of gadolinium has been linked to the development of nephrogenic systemic fibrosis in patients with advanced renal failure, in particular patients on dialysis and is contraindicated in this patient group.

PET-CT with ¹⁸F-FDG has been reported to be a useful imaging modality to demonstrate areas of systemic amyloid deposition. Cases of amyloid arthropathy in patients with multiple myeloma and light-chain amyloidosis diagnosed with ¹⁸F-FDG PET-CT have been described.^{7, 8} Our case complements these reports in showing the utility of ¹⁸F-FDG PET-CT in the diagnosis of amyloid arthropathy secondary to DRA, which is particularly useful in this patient population due to the contraindication to gadolinium which renders MRI evaluation suboptimal. ¹⁸F-FDG PET-CT represents a non-invasive imaging modality which can be of value when conventional radiographs are not helpful in establishing the diagnosis or when disease extent is underestimated in patients with suspected amyloid arthropathy.

The authors have no conflicts of interest

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“NO TIME FOR TEACHING AT OUR TEACHING HOSPITALS.”

Editor,

Depending on the speciality choice you have made you may

spend anywhere between zero and one hundred percent of your direct clinical contact time in an outpatient setting. The UK Patient charter, now designated the NHS Constitution, sets out the standards of care that patients can expect including the maximum waiting time for a routine outpatient appointment which currently stands at 18 weeks in the United Kingdom¹. Within Otorhinolaryngology outpatient referrals have increased year on year. With increasing referral numbers and fixed waiting times outpatient clinics are at risk of being overloaded with decreasing time available for patients to spend with their doctor and potential decreases in the quality of care that they may obtain.

ENT UK have drawn up guidelines for safe patient numbers at clinics for consultants, registrars, SAS and junior trainees². No such guidelines are present for other specialities. Mention is made in the ENT UK guidelines with regards to reducing clinic numbers for consultants supervising trainees, however no mention is made with regards to medical student teaching for either consultant or registrar grades.

In 1845 the number of students studying medicine at Queens University was 55, while today the number of full-time students is approximately 1200³. This is a substantial increase and is common across all Universities in the UK. Interestingly a review into admission rates to Medical and Dental Schools in the UK has shown that admissions have exceeded recommendations for at least the past five years and the government have recommended a 2 per cent reduction in intakes from next year⁴.

This increasing number of medical students will all engage in clinical tuition to some extent throughout their undergraduate career with a proportion of this occurring in the outpatient setting. A study in 1999 suggested that medical student satisfaction is higher when they have the opportunity to both sit in on consultations and get an opportunity to take histories and certainly this is a key aspect of medical training⁵. The slow erosion of supporting profession activities (SPA) sessions is resulting in the relocation of medical student teaching from non clinical sessions into clinical time. Unfortunately this places additional demands on the supervising doctors in these clinics to provide both high quality patient care and tuition and one would question whether this well versed form of teaching is sustainable. In addition medical school admissions are increasingly competitive as are foundation job placements which has led to increased student expectations and demand for a greater duration of higher quality teaching.

Increasingly teaching is being diluted in our teaching hospitals to allow the prioritization of service provision. In an era of increasing litigation, time pressure and patient demand we need to ensure that our clinics are productive, safe, sustainable and provide adequate learning opportunities for medical students and junior doctors. This may mean that patients numbers at outpatient clinics need to be reduced to ensure successive doctors remain competent to treat them.

The authors have no conflict of interest.

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ACUTE FULMINANT NECROTISING LYMPHOCYtic MYOCARDITIS IN A PATIENT WITH MIXED CONNECTIVE TISSUE DISEASE: A RAPID CLINICAL RESPONSE TO IMMUNOSUPPRESSION

Editor

Myocarditis is an uncommon condition encompassing a spectrum from asymptomatic cases to fulminant heart failure. Acute fulminant myocarditis is characterised by severe haemodynamic compromise often necessitating circulatory support. The diagnosis and management of myocarditis remains challenging with uncertainty surrounding the role of immunosuppression therapy. We describe a case of biopsy-proven acute necrotising lymphocytic myocarditis which responded rapidly to steroids, mycophenolate and immunoglobulins.

A 53 year old male was admitted to a District General Hospital with a 4-day history of chest pain and 'flu-like symptoms. He had a history of mixed connective tissue disease (MCTD). Physical examination revealed sinus tachycardia (126bpm) and mild pulmonary oedema.

The ECG on admission showed sinus rhythm with Q waves in the anterior chest leads and T wave inversion in leads I, aVL and V3-V6. High-sensitivity troponin T (hsTNT) was 5220ng/L and the C - reactive protein (CRP) was 328mg/L. Within 24 hours he developed cardiogenic shock with severe pulmonary oedema, left bundle branch block and severe left ventricular systolic dysfunction (LVSD). Transfer was

arranged due to clinical instability. At cardiac catheterisation, the aortic pressure was 83/55mmHg with a left ventricular end-diastolic pressure of 35mmHg. Coronary angiography showed no obstructive disease and an intra-aortic balloon pump (IABP) was sited.

With the progressing ECG abnormalities, echocardiographic findings and rising biomarkers, a diagnosis of acute myocarditis was made. Urgent right ventricular endomyocardial biopsies were undertaken with frozen section analysis confirmed acute necrotising myocarditis. There was no evidence of vasculitis and giant cells were absent on histopathology (Figures 1 & 2). Immunohistochemistry was negative for Epstein Barr virus (EBV) and parvovirus. Viral polymerase chain reaction (PCR) was weakly positive for both. Screening for hepatitis B, C, cytomegalovirus (CMV), erythrovirus B19, streptococcus pneumoniae and picornavirus was negative.

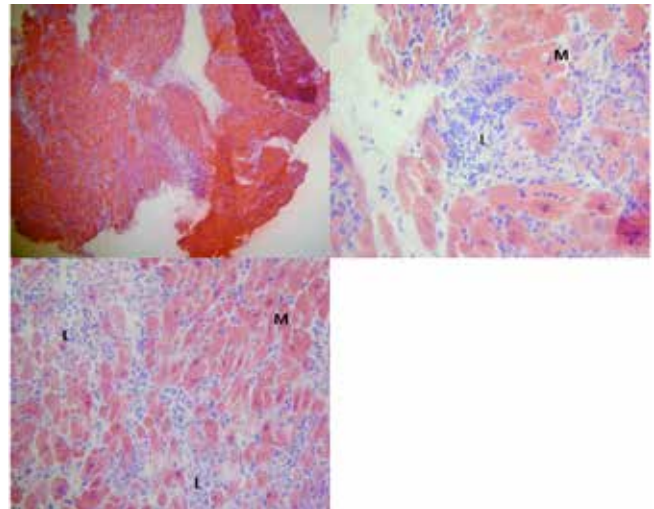


Fig 1. Histology specimen from the endomyocardial biopsy demonstrating myocardium with a dense infiltrate of inflammatory cells (L)-(dark blue nuclei) separating the myocytes (M)

Oral prednisolone (40mg OD) and mycophenolate mofetil (500mg BID) were commenced on rheumatological advice. A total dose of 300g of Human Immunoglobulin [Privigen® (CSL Behring, PA, US)] was administered over 5 days.

A rapid clinical improvement ensued, facilitating IABP removal and discontinuation of inotropes after 72 hours. Standard heart failure therapy was commenced. Repeat echocardiography by day 9 showed only mild global left ventricular systolic impairment. Temporary interruption in mycophenolate therapy occurred due to shingles (treated with Ganciclovir). He was discharged on day 15.

DISCUSSION

The diagnosis of myocarditis should be considered in any patient presenting with acute heart failure. Non-invasive imaging modalities (ECHO and Cardiac MR) are helpful in establishing the diagnosis. Ultimately, myocarditis is a histopathological diagnosis. Multiple endomyocardial biopsy samples are required as sampling error can occur in the setting

of patchy disease. The most common histopathological form of acute myocarditis is a lymphocytic pattern. The mainstay of treatment in acute myocarditis is inotropic agents and circulatory support. The efficacy of intravenous immunoglobulin (Ig) and immunosuppression remains unproven. Studies have demonstrated mortality benefits with early IG and steroid administration.

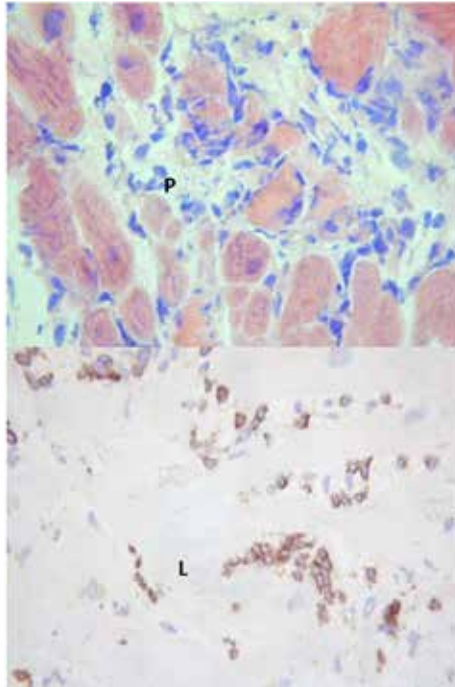


Fig 2. Histology specimen from the endomyocardial biopsy demonstrating extensive myocyte necrosis and phagocytosis (P). Immunohistochemistry has been performed highlighting the T lymphocytes (L)

The authors have no conflicts of interest

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MOLECULAR PROFILING OF GLIOMAS - TIME FOR A REGIONAL SERVICE.

Editor,

Gliomas form a heterogeneous group of intrinsic primary brain neoplasms in terms of pathological and clinical features.¹ Low-grade (WHO grade II) gliomas (e.g. astrocytomas and oligodendrogliomas) inevitably recur and progress to higher grade (WHO III-IV) anaplastic tumours. Although they have traditionally been classified using histological criteria, there is increasing evidence that gliomas can be further subtyped

based on molecular profile which can predict prognosis and response to treatment.²

Longterm follow-up data has demonstrated a significant survival advantage with anaplastic oligodendroglioma (AO)/oligoastrocytoma (AOA) tumours co-deleted for chromosomal arms 1p and 19q following combined chemo-radiotherapy compared with non-1p19q codeleted cases. These findings validated in both European (EORTC 26951)³ and North American trials (RTOG 9402)⁴ have meant that 1p19q status predicts post-surgical treatment. The current standard of care is that co-deleted cases receive chemoradiotherapy while non-deleted cases receive only radiotherapy due to the lack of efficacy of combined treatment in this group.

Prior to this recent change in practice, all patients with anaplastic oligodendroglial tumours were treated with radiotherapy upfront and received chemotherapy (typically procarbazine, lomustine and vincristine) on relapse. The aim of this regional retrospective study was to establish as a baseline NI clinical outcomes using this pre-1p 19q stratification as a comparator for future outcomes studies.

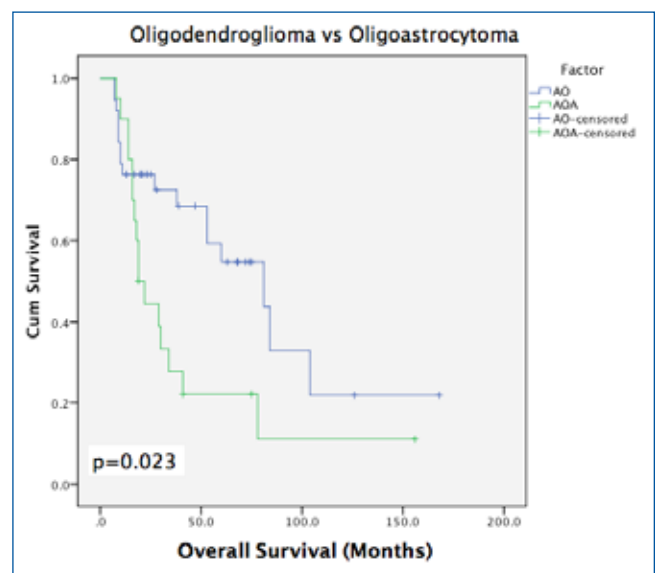


Fig 1. Kaplan-Meier survival curves for anaplastic oligodendroglial (AO) versus anaplastic oligoastrocytoma patients treated in NI over a 5-year period (2007-2012).

RESULTS

Clinical, pathological and molecular profile data (available in 20 cases) were analysed in 58 consecutive patients with a histological diagnosis of anaplastic oligodendroglial tumour diagnosed over a five-year period (2007 to 2012). The median survival of all patients was found to be 53 months (95% CI 22-84 months). The median survival of patients with AO (n=38) was found to be 81 months (95% CI 37-125 months). The median survival of patients with AOA (n=20) was found to be 19 months (95% CI 14 to 25 months). Log-rank analysis confirmed that AO patients had a significantly longer median survival than those with AOA tumours (p=0.023) comparable with other reports (Fig. 1).⁵

Patients with the 1p/19q co-deletion (n=13) had a median survival of 74 months (95% CI 21-127 months), while those without the co-deletion (n=7) had a median survival of 60 months (95% 47-74 months) although the difference was not significant to the small size of this preliminary dataset (p=0.782).

DISCUSSION

Our review of anaplastic oligodendroglial tumours treated “pre-1p19q stratification” indicates our clinical outcomes are comparable with other published reports. This study serves as an important baseline for future comparative studies following the recent change in practice. It is also a requirement of ongoing national cancer peer review to report regional outcomes for patients and benchmark them with the national standards. Furthermore, with the emergence of molecular profiling of all gliomas as a mandatory requirement in the forthcoming amended WHO diagnostic criteria, it will be important to have access to a regional service that can provide molecular profile in tandem with routine histology reports. Not only will this ensure our patients receive the same standard of care as other UK neuro-oncology centres but also minimise anxiety associated with delays in molecular profile reports returning from outside institutions.

The authors have no conflict of interest apart from the pressing clinical need of a regional molecular profiling service.

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A SHOTGUN INJURY TO THE BUTTOCKS; GETTING TO THE HEART OF THE MATTER.

Editor,

CASE:

A 19-year-old male presented with a shotgun injury to the buttocks. Entry wounds were visible on both buttocks. There were no other wounds. A pelvic radiograph revealed multiple pellets projected over the right hemi-pelvis (Figure 1). A chest radiograph demonstrated two small foreign bodies in the region of the right heart (Figures 2 and 3). Subsequent computed tomography showed extensive shrapnel in the right transgluteal and perineal regions and two pellets embedded in the right atrium. This embolisation is attributable to entry into the circulation via the pelvic venous system. The patient underwent debridement of the buttock wounds. An echocardiogram excluded a patent foramen ovale. No attempt was made to retrieve the embolised pellets and the patient has remained asymptomatic.



Fig 1.

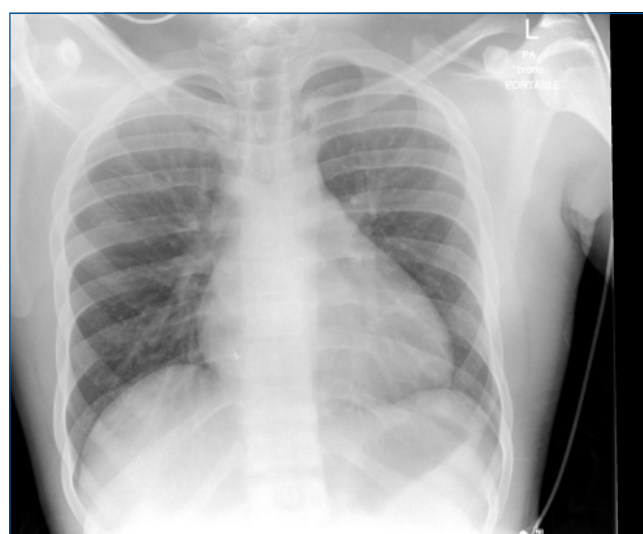


Fig 2.

DISCUSSION:

Foreign body embolisation is a rare complication of penetrating trauma from firearms. The incidence of bullet embolisation after penetrating injury is estimated to be 0.3 – 1% (1). Patients may be asymptomatic, however the development of complications such as distal limb ischaemia, endocarditis, pulmonary embolism or stroke should prompt consideration of emboli. The diagnosis of bullet embolisation should also be considered when there is a discrepancy between the number of penetrating wounds and the foreign bodies identified, the location of the bullet does not match that which would be expected by the trajectory or when migration of bullets are demonstrated on serial radiographs.



Fig 3.

The most common destination of venous emboli is the right ventricle followed by the pulmonary artery. Embolisation to the right atrium represents less than 5% of the final destination of all such emboli (2). The most common destination of

bullet emboli within the arterial system is the femoral artery. The main risk associated with venous emboli is pulmonary embolism, however arterial complications may still occur from right heart emboli if a patent foramen ovale is present. The incidence of patent foramen ovale in the general population is estimated at 25% (3). Emboli in the arterial system are symptomatic in 80% of cases compared to 33% of venous system cases (4).

Foreign bodies that embolise to and remain within the heart have been managed both conservatively and surgically in the literature (5). There may be a role for percutaneous intervention in some cases, however this has not been explored in detail. The presence of complications including endocarditis or arrhythmias may be an indication for intervention. Intra-cardiac emboli may be entrapped within endocardial trabeculations and with time can become encapsulated within fibrous tissue. The long-term risks of endocarditis or mural thrombus formation are not known.

CONCLUSION:

Foreign body embolisation should be considered in patients presenting with unexpected symptoms, signs or radiological findings following firearms injury. An echocardiogram should be performed for right heart emboli to exclude a patent foramen ovale due to the risk of arterial embolisation.

The authors have no conflicts of interest

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