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CASE REPORT

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Achromobacter xylosoxidans totally implantable venous access device infection in a person with cystic fibrosis: Complex management considerations

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Abstract

Totally implantable venous access devices (TIVADs) are frequently used in people with cystic fibrosis as a means of securing consistent vascular access, particularly in the context of severe disease and microbial colonization. Infection of TIVADs is not uncommon and typically associated with coagulase negative staphylococci, though infection with other organisms does occur too. We report on the first case of a TIVAD infection caused by *Achromobacter xylosoxidans* in person with cystic fibrosis. The TIVAD infection was complicated by a bacteraemia and an associated intracardiac infected thrombus at the superior atriocaval junction. We explore the complex management decisions surrounding the removal of the TIVAD and prolonged antibiotic treatment, with treatment ultimately resulting in a good outcome and full recovery. The case helps to serve as a timely reminder of requirement to review the necessity to retain TIVAD in the era of CFTR modulator therapy and associated improved health outcomes being experienced.

KEYWORDS
cardiovascular medicine, cystic fibrosis, infection and inflammation

INTRODUCTION

Totally implantable venous access devices (TIVADs) have been in use in people with cystic fibrosis (pwCF) for several decades, as a means of securing consistent vascular access.[1] Infection of TIVADs is not uncommon, with blood stream infections (BSI) predominantly reported to be caused by coagulase negative staphylococci.[2,3] Whilst there are case reports of rare organisms causing TIVAD associated BSI, including *Mycobacterium avium*,[4] there have only been very limited reports of *Achromobacter xylosoxidans* associated BSI in immunocompetent people, and none in pwCF.[5–7] Typically *A. xylosoxidans* BSI are associated with central venous catheters in people immunodeficiency, particularly neutropenia.[6,7] There has also been an isolated report of outbreaks in a haemodialysis unit where it could be argued that a significant risk factor to consider would be the degree of immunodeficiency owing to end-stage renal failure.[8] Whilst *Achromobacter* species (sp.) have generally been increasingly recognized as concerning respiratory pathogens in pwCF associated with severe disease outcomes due to significant intrinsic antibiotic resistance, association with TIVAD infections has not been previously reported.[9] We described the first reported case of a TIVAD infection caused by *A. xylosoxidans* in an immunocompetent pwCF and the management challenges encountered with this rare infection.

CASE REPORT

We report on the complex management decisions of a 24-year-old female with cystic fibrosis (F508del/F508del). She had severe lung disease alongside CF-related diabetes (CFRD), chronic rhinosinusitis and nasal polyps, CF-related liver disease (CFLD) and osteopenia. Her FEV1 at baseline was around 1.40 (42% predicted). Owing to her severe phenotype, profound needle phobia and colonization with *Pseudomonas aeruginosa*, a TIVAD had been sited during

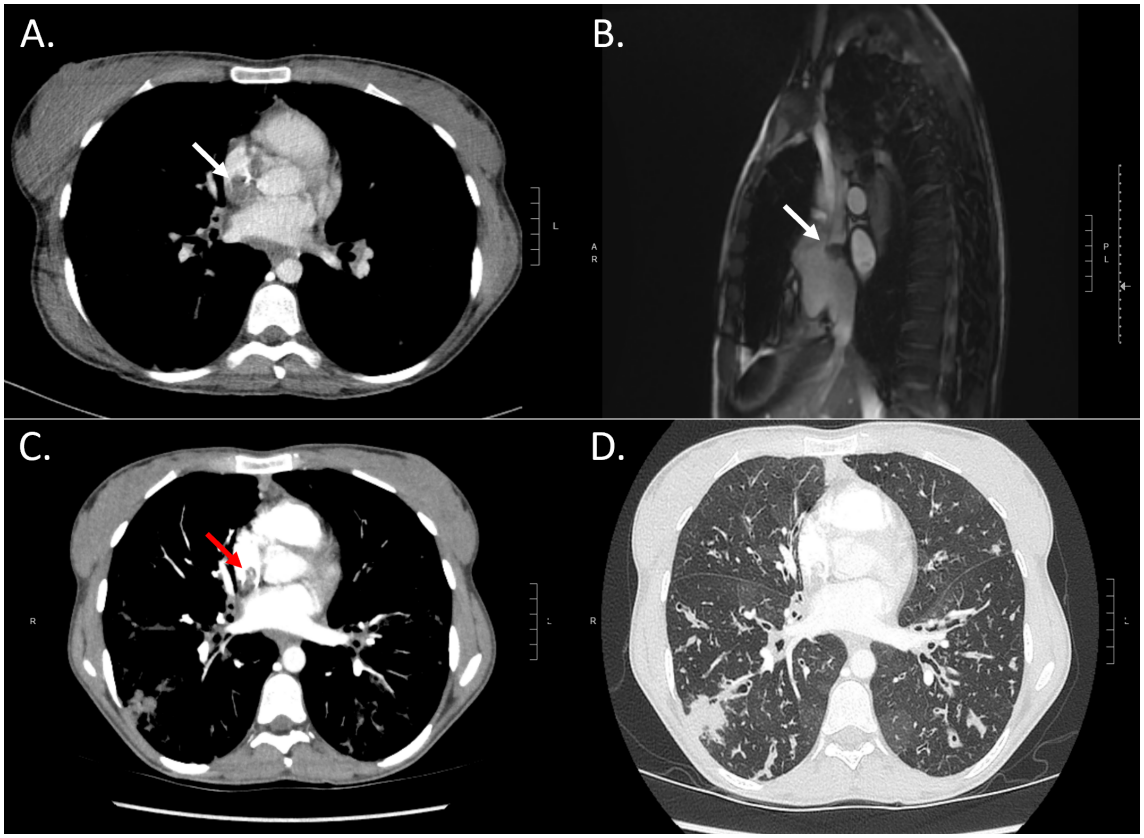

FIGURE 1 (A) Computed tomography chest highlighting retained totally implantable venous access devices (TIVAD) segment with associated filling defect (white arrow) at the tip. (B) Cardiac MRI highlighting the same retained TIVAD segment with associated thrombus (white arrow) appearing adherent to the posterior surface of the right atrium. (C) CT pulmonary angiogram (CTPA) showing lobulated superior atriocaval junction thrombus (red arrow) with right lower lobe subpleural multifocal consolidation associated with right lower lobe segmental and left lower lobe subsegmental pulmonary emboli (PE). (D) CTPA lung windows highlighting subpleural consolidation and underlying bronchiectasis.

paediatric care at the age of 9 years to aid management of frequent infective pulmonary exacerbations.

Following admission in 2016 for management of an infective exacerbation of CF caused by *P. aeruginosa*, she was commenced on intravenous antibiotics in the form of ceftazidime and tobramycin. Shortly after initiation of these antibiotics she developed a pyrexia (38.9°C) that coincided with access and initial use of her TIVAD. Both peripheral circulation and central blood cultures, obtained from the TIVAD, cultured *A. xylosoxidans* after 48 h of growth. This organism exhibited extensive resistance to co-trimoxazole, gentamicin, tobramycin, ceftriaxone, ceftazidime and meropenem, but was sensitive to piperacillin/tazobactam. She was therefore commenced on intravenous piperacillin/tazobactam, continued alongside ceftazidime and tobramycin initially commenced as treatment of her pulmonary exacerbation. The decision was made to surgically remove the TIVAD following this, but unfortunately removal was complicated by a line fracture with part of the catheter remaining in situ and unable to be extracted intraoperatively. Venous access was maintained via the insertion of a peripherally inserted central catheter (PICC) line. A computed tomography (CT) scan of chest demonstrated the retained portion of the TIVAD within a high-grade stenosis/occlusion of the distal right subclavian vein with extensive associated collateralisation (Figure 1A). A filling defect at the tip of the retained TIVAD segment was noted and felt to be consistent with associated thrombus. Further evaluation of the suspected thrombus was carried out with echocardiogram followed by cardiac magnetic resonance imaging (MRI) (Figure 1B).

Given the presence of a suspected thrombus, treatment with IV heparin was initiated. However, despite ongoing treatment with the combination of IV antibiotic therapy and IV heparin, her clinical condition failed to improve associated with ongoing intermittent fevers.

The decision was made to remove the retained segment due to concerns regarding the possibility of an *Achromobacter* associated infected thrombus. The options of open cardiac surgical excision and percutaneous removal of the retained segment were considered. The potential for a catastrophic intraoperative vascular event such as rupture of the right atrium, and the option of a combined heart-lung transplant in the event of such a scenario, were discussed with both the pwCF and her family. Ultimately, percutaneous removal under a general anaesthetic was the preferred option owing to the inherent risks of cardiac surgery and the pwCF's preference not to proceed to potential transplantation in the event of a catastrophe. The retained catheter segment was removed without any immediate intra-procedure complications.

Subsequent microbiological analysis of the TIVAD line tip also yielded growth of *A. xylosoxidans*. Unfortunately, her post-operative recovery was complicated by worsening fevers and haemodynamic instability. Subsequent imaging with CT pulmonary angiography highlighted probable septic emboli determined to be the result of a septic shower secondary to removal of the infected thrombus (Figure 1C,D).

Gradual clinical improvement was observed over the course of the next 2 weeks with ongoing treatment with IV piperacillin/tazobactam and anticoagulation in the form of subcutaneous enoxaparin. In total, 6 weeks of IV antibiotic therapy was administered following removal of the retained TIVAD segment. A major determinant of the length of treatment was the fact that most of the thrombus associated with the removed line tip remained in situ at the atriocaval junction adherent to the atrial wall as demonstrated by further cardiac MRI imaging. Anticoagulation was eventually switched to rivaroxaban and continued on discharge from hospital for a total of 6 months, with sequential cardiac MRI scans showing gradual resorption of the thrombus until its near total resolution 13 months after removal of the retained TIVAD segment. This coincided with a complete resolution of her clinical symptoms and no recurrence of pyrexia or bacteraemia on serial testing up to four months after the initial positive blood cultures.

DISCUSSION

Achromobacter sp. are increasingly recognized as an opportunistic pathogen of concern in pwCF.[10] A recent review of the European CF Society Patient Registry reported isolates of *Achromobacter* sp. in 2093 pwCF with a prevalence of 5.4%. Features contributing to isolation included minimal function *CFTR* mutation classes; poor nutritional status; lower pulmonary function; and previous use of inhaled antibiotics targeting *P. aeruginosa*.[9] Whilst our pwCF had a significant number of these features including low body mass index (BMI), 18–19.24 kg/m^2, reduced FEV1 and previous use of nebulised tobramycin, *Achromobacter* sp. had never been isolated from her sputum. This suggests that her TIVAD infection and associated bacteraemia most likely resulted from direct contamination at a previous time of access, particularly given *Achromobacter* sp. ubiquitous presence in aquatic environments and soil,[10] only coming to light at subsequent use.

Concern regarding *Achromobacter* sp. as a respiratory pathogen has been increasing. All the case reports in the literature detailing infection prior to 2014 have been of a pulmonary nature, while more recently there has been increasing recognition of *Achromobacter* sp. in other settings such as soft tissue or surgical wound infections, particularly but not exclusively, in immunocompromised people.[5–7,11] However, to date there have only been very limited reports of line associated infections in immunocompetent people. Whilst previous reports of *Achromobacter* sp. BSI tend to favour underlying risk factors for immunosuppression such malignancy, documented neutropenia, and/or concurrent steroid use,[6,7] there have been a select number of cases where no reported immunocompromise was found. However, none of these cases have been in a pwCF. Whilst it could be argued that our pwCF exhibited a severe phenotype, including CFRD, likely to have impacted her immune function, this case is uniquely different to the context of immunosuppression secondary to malignancy, neutropenia or pharmacotherapies found in other reported instances. Despite these differences in risk factors, extra vigilance should be observed in the context of managing pwCF with severe phenotypes owing to their vulnerability to these types of opportunistic infections.

Antibiotic treatment duration was by necessity prolonged in this case owing to the residual infected thrombus in the right atrium. Fortunately, there was a favourable outcome, but the resistance profile of the *Achromobacter* sp. in our case was concerning, particularly its resistance to carbapenems. *Achromobacter* sp. containing two main intrinsic resistance mechanisms comprising of multidrug efflux pumps and chromosomal OXA-114-like β-lactamases.[12] This, coupled with frequent antibiotic allergies or intolerances in pwCF, can often prove a major barrier to effective treatment implementation.

The frequency of TIVAD associated infections and BSI in the era of CFTR modulator therapy remains unknown with no current publications available relating to this. Whilst most pwCF are seeing improved health outcomes with CFTR modulator therapy, there remain a significant proportion of pwCF who retain TIVADs for ongoing management in the setting of advanced lung disease and/or frequent exacerbations. Associated factors that potentially govern the risk of TIVAD complications have been identified as lower baseline FEV1, CFRD and frequent pulmonary exacerbations, presumed secondary to increased use and access of TIVADs.[13,14] Though it is worth noting that there are also large cohort studies indicating no obvious risk factors for the development of TIVAD infections.[15] Potential factors to consider when trying to mitigate the risk of the development of TIVAD infections could therefore involve the optimisation of diabetic control whilst also ensuring optimisation of general treatments aimed at slowing the rate of FEV1 deterioration. One would therefore expect an overall reduction in the rates of TIVAD associated infections associated with the introduction of CFTR modulator therapy given most pwCF experience improvements in lung function with initiation of this treatment. Additionally, increased rates of TIVAD removal owing to improving health outcomes will likely result in a global reduction in TIVAD infections. However, despite this, the risk of TIVAD associated infection remains in those pwCF retaining them for ongoing clinical use. For those pwCF who still have TIVADs in situ, ongoing review of the risk–benefit ratio of leaving these devices in place forms one of many complex ongoing management decisions, particularly when they have been in place long term. The TIVAD infection in this case occurred prior to our pwCF receiving modulator therapy, with her now established on elexacaftor/tezacaftor/ivacaftor and exhibiting improved lung function (FEV1 2.09, 64% predicted). None-the-less, her case forms a

timely reminder of the risks relating to TIVADs and BSIs, particularly with rare organisms not regularly encountered in clinical practice.

In summary, we provide the first description of *A. xylosoxidans* bacteraemia associated with a TIVAD in a pwCF and highlight the complexities of management decisions relating to this infection, particularly related to the TIVAD associated infected intracardiac thrombus. Vigilance should be maintained despite improved health outcomes with CFTR modulator therapies and the decisions around whether to consider TIVAD removal made on an individual basis based on the perceived risk–benefit analysis.

AUTHOR CONTRIBUTIONS

Ieuan E. S. Evans and David Reid were involved in conceptualizing the case report with Ieuan E. S. Evans writing the article with contributions from David Reid. Haris Haqqani, Daniel Smith, and David Reid were involved in the inpatient care over the duration of his hospital admissions. All authors involved in critically reviewing and editing the report and all have provided final approval for publication.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

No data available.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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