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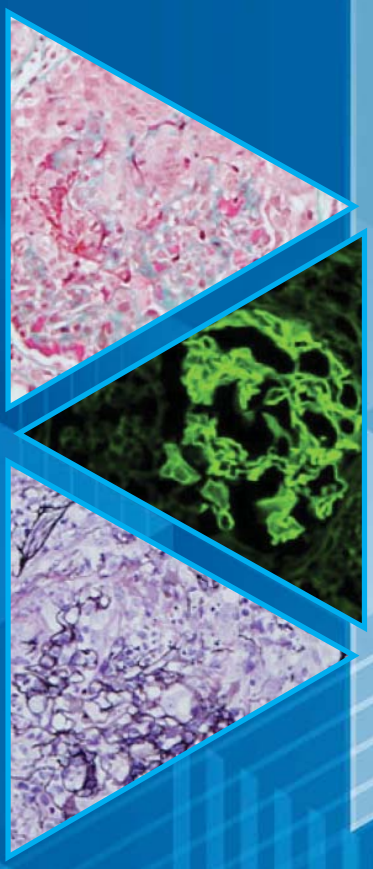

Original Articles

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Editorial Open Access

ACTINOMYCES ODONTOLYTICUS CATHETER RELATED BLOODSTREAM INFECTION IN A HEMODIALYSIS PATIENT - FIRST REPORTED CASE

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ABSTRACT

Actinomyces odontolyticus is a gram-positive bacillus, usually found in oropharynx, gastrointestinal tract and urogenital tract as human commensal flora. Infection caused by this organism is rare but may occur in an immunocompromised patient. This organism has been known as difficult to be cultured. We reported a case of 60 years old woman, on regular hemodialysis for the past 3 years, who had *Actinomyces odontolyticus* bacteremia due to catheter-related bloodstream infection. She was treated with antibiotics for 3 weeks and was referred to the dentist for dental clearance. We believe this is the first case report of *Actinomyces odontolyticus* bacteremia in a hemodialysis patient. This case report highlighted the importance of looking for the primary source (in this case oral cavity) as this is usually an endogenous infection arising most frequently from the mucosal membrane. Early eradication of the primary source may help to fasten the recovery and prevent it re-occurs in the future.

Keywords: *Actinomyces odontolyticus*, bacteremia

INTRODUCTION

Actinomyces odontolyticus is an anaerobic, gram-positive bacteria. Other characteristics include facultative capnophilic, nonsporulating, non-motile and usually stained irregularly (1). It was first discovered by Batty (2) in 1958, where he isolated this organism from a person with advanced dental caries. *Actinomyces odontolyticus* infections are rare, presenting an endogenous infection arising commonly from mucous membranes (3). Other reported sources included soft tissue, lung, abdomen and pelvic region (1). Although the prognosis of the infection caused by this organism is generally good with medical therapy, it still can lead to death if proper treatment is not initiated early (3). Here we reported a case of *Actinomyces odontolyticus* bacteremia due to catheter-related bloodstream infection, which is yet to be reported in the literature.

CASE REPORT

This is a 60 years old woman, diagnosed to have End-stage renal disease (ESRF) since 2016, on regular hemodialysis via right brachiocephalic fistula (BCF). In May 2019, her BCF was thrombosed and temporary right internal jugular catheter (IJC) was inserted for hemodialysis on 9th May 2019. Since then she had multiple hospital admissions mostly due to catheter malfunction and multiple catheter exchanges were done throughout the hospitalizations.

On 9th September 2019, she was again admitted to hospital. This time she complained of fever for 1 day associated with chills and rigours during hemodialysis. During the physical examination, pus discharge was noted from the catheter insertion site. A swab from the exit site and blood culture were taken and ceftazidime and cloxacillin were started. The previous catheter was taken out and a femoral catheter was inserted as temporary dialysis access. Her blood investigations showed leucocytosis with predominantly neutrophils (66% of total white cell counts). Her fever settled down the next day. Gram staining for swab culture showed numerous gram-negative rods but blood culture showed gram-positive cocci in a cluster.

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Cloxacillin was stopped and switched to cefazolin due to difficult venous access, but ceftazidime was continued. She remained well throughout the hospitalization. Swab culture showed no growth after 3 days of incubation though initial gram staining able to identify gram-negative rods organism. After 5 days of admission, her aerobe blood culture showed methicillin-resistant coagulase-negative Staphylococcus (MRCONS) whereas both peripheral and central anaerobe blood culture, which was released after 10 days, showed *Actinomyces odontolyticus*. MRCONS was not treated as the patient responded well to the antibiotics. The antibiotic was subsequently changed to Intravenous (IV) Augmentin after discussion with the microbiologist. She was then referred to the dentist for dental clearance as this organism commonly colonized the oral cavity. She was diagnosed to have chronic generalised periodontitis. Full mouth scaling and filling was done for the cervical abrasions of right upper canine, left upper central incisor, left lower central incisor, left lower first premolar and right lower central incisor of teeth. Teeth extraction were done for left upper first molar and right lower first premolar. She was remained well and afebrile since started antibiotics. Her white cell counts and C-reactive protein coming down eventually throughout the admission. We continued the IV Augmentin for another 11 days with total of 3 weeks duration of antibiotics.

Due to the patient's poor vascular access, counselling was done for conversion to peritoneal dialysis. A peritoneal dialysis catheter was inserted after completed antibiotics for 3 weeks and she was currently well receiving peritoneal dialysis treatment.

DISCUSSION

Actinomycosis is a rare chronic disease caused by *Actinomyces* spp which normally colonize the human mouth and digestive and genital tracts. More than 30 species of *Actinomyces* have been described so far. The most common Actinomyces spp isolated in human infections is *Actinomyces israelii*, and is found in most clinical forms of actinomycosis (4). Whereas *Actinomyces odontolyticus* is mostly found in mouth, oropharynx and upper gastrointestinal tract. This organism is one of the most prevalent *Actinomyces* spp that take part in forming a biofilm on teeth at all ages (5). Infections caused by *Actinomyces odontolyticus* are rarely found, more frequently affecting middle-aged males and immunocompromised patients (3). Clinical features of actinomycosis can be varied, depends primarily on the site/organ involvement. Cervicofacial and abdominopelvic location will be the commonest site, followed by pulmonary and digestive tract. Even central nervous system actinomycosis was reported before (4).

The culture of *Actinomyces* is quite difficult as *Actinomyces* infections are likely to be polymicrobial due to previous exposure to antibiotic therapies. More time is usually needed to culture *Actinomyces* in an anaerobic environment (5). It usually appears in blood culture after at least 5 days and sometimes may take up to 15–20 days. Thus, incubation of at least 10 days is required before confirmation of a negative culture (4). Small, irregular, whitish colonies that are smooth to slightly granular will be seen in blood agar and dark red pigment will appear when mature (2–14 days). *Actinomyces odontolyticus* shows negative catalase and oxidase tests. It reduces nitrates to nitrites and does not grow at pH 5.5 (1). As for treatment, *Actinomyces spp* is usually extremely susceptible to beta-lactams antibiotics as it does not produce beta-lactamase. Thus, penicillin G or amoxicillin is the recommended initial therapy for the treatment of actinomycosis (4). Nevertheless, prolonged therapy with high doses of antibiotic is usually required to ensure adequate antibiotic penetration of the primary source of infection. Surgical intervention may be needed, especially those with abscess or widespread necrotic tissue (5).

In our case report, we think that the most likely source of bacteremia is from the chronic periodontitis as this patient had poor oral hygiene. Although this organism is a commensal in the oral cavity, it might still cause bacteremia especially in an immunocompromised patient like ours. However, we were not able to identify the exact mode of transmission to the catheter. The possible postulation is that the bacteria might colonize the catheter through blood transmission. We referred her to the dentist immediately once the blood culture result was released and dental clearance was done promptly in an attempt to eradicate the source of infection.

CONCLUSION

Actinomycosis is a rare disease caused by *Actinomyces spp*, and it can be easily missed as it is not easy to be cultured. While actinomycosis is easily treatable with common broad-spectrum antibiotics, it may still cause a fatal outcome if it is not recognized early or treated with an inadequate dose or duration of antibiotics. Eradication of the primary source is the cornerstone of the treatment. In our case, treatment with appropriate antibiotics and prompt referral to look for primary source fasten the recovery of this patient. This case high lightened the importance of knowing the common source of rare organism and thorough oral cavity examination must be carried out whenever actinomycosis is suspected.

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Editorial

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DOUBLE POSITIVE ANTI-GBM AND ANCA-ASSOCIATED GLOMERULONEPHRITIS – A CASE REPORT

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ABSTRACT

Double-Positive Anti-Glomerular Basement Membrane (Anti-GBM) and Anti-Neutrophil Cytoplasm Antibody (ANCA)- Associated Glomerulonephritis is a rare disease. The disease is characterized by the concurrent presence of Anti-GBM antibodies and ANCA in a patient. The patient usually presents with rapidly progressive glomerulonephritis with or without pulmonary haemorrhage. We report a case of a middle-aged gentleman who presented with acute kidney injury with a serum creatinine level of 459umol/L. He tested positive for both Anti-GBM and ANCA with high titers. He underwent 8 cycles of plasma exchange, pulse IV cyclophosphamide, and high dose steroids. At the time of review at 6 months, a total of 6 doses IV cyclophosphamide had been given and his serum creatinine had recovered to 146 umol/L with the eGFR of 42ml/min. Although there is no published literature to date on the use of IV cyclophosphamide as compared to oral cyclophosphamide for the initial immunosupressive therapy, the encouraging response in this patient suggests that it could be an alternative to oral cyclophosphamide to reduce overall immunosuppressive load.

Keywords: ANCA, Anti-GBM, vasculitis

INTRODUCTION

Double-Positive Anti-Glomerular Basement Membrane (Anti-GBM) and Anti-Neutrophil Cytoplasm Antibody (ANCA)-Associated Glomerulonephritis is a very rare disease with an incidence of less than one per million population. The disease is characterized by the concurrent presence of Anti-GBM antibodies and ANCA in a patient presenting with rapidly progressive glomerulonephritis with or without pulmonary haemorrhage. It has been previously reported that up to 50 per cent of patients with Double-Positive Anti-Glomerular Basement Membrane (Anti-GBM) and Anti-Neutrophil Cytoplasm Antibody (ANCA)-Associated Glomerulonephritis became dialysis dependent (1).

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CASE REPORT

We report a case of Double-Positive Renal-Limited Anti-GBM disease in a 59-year-old gentleman. The patient, who was a smoker, presented with a history of dry cough and intermittent fever over one month. There was no history of haemoptysis or reduced urine output. The patient has underlying chronic obstructive airway disease in which he requires two types of inhalers for disease control. He also has type 2 diabetes mellitus currently controlled by tablet vildagliptin 50mg once daily. He worked as a truck driver. Physical examination showed the presence of moderate lower limb oedema but was otherwise unremarkable. His blood pressure on admission was 145/64, pulse rate was 67, and the temperature was 37-degree Celcius.

Initial blood investigations showed hemoglobin 8.7 g/dL (normal range 13.0 - 17.0 g/dL), total white blood cells 5.6 x109 /L (normal range 4.0 - 10.0 x109 /L), platelet 343 x 109 /L (normal range 150 – 410 x109 /L), urea 10.3 mmol/L (normal range 2.76-8.07 mmol/L), creatinine 256 µmol/L (normal range 62- 106 µmol/L). The full blood picture was not performed. Twenty-four-hour urine protein was 1.8g/day. His renal function deteriorated rapidly, with a rise in creatinine to 459 µmol/L on day 3 of presentation.

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Serology for autoimmune workup revealed Antinuclear Antibody (ANA) positive with a titre of 1:160, Anti-Double Stranded DNA was negative, p-ANCA positive with a titre of 1:320 and Anti-GBM antibody positive with a titre of >200 IU. Anti-Myeloperoxidase antibody (MPO) and Anti-Proteinase-3 (PR-3) antibodies were not performed. His serology testing for hepatitis B, hepatitis C and HIV were negative. Lung involvement was ruled out by the presence of clear lung fields on chest radiography and high resolution computed tomography of the thorax. Ultrasound of the abdomen showed normal echogenicity of the bilateral renal parenchyma. The size of the right kidney on ultrasound was 11.9cm and left kidney was 12cm. Urgent renal biopsy on day 3 of the presentation showed 22 glomeruli with 64% fibrinoid necrosis of the glomerular tufts and the presence of cellular crescents in 59 % (Figure 1 & 2). Immunofluorescent staining of the renal biopsy specimen revealed linear IgG (3+) positivity along the glomerular basement membrane (Figure 3).

The patient was given pulse intravenous methylprednisolone 500mg for 3 days followed by 8 cycles of plasma exchange at 1.5 times plasma volume replaced by FFP for 2 weeks. At 2 weeks, his serum creatinine improved to 300 µmol/L. The serum Anti-GBM antibody titre decreased to 84 IU/L. Proteinuria reduced to 0.5g/day. Repeated p-ANCA was negative. Subsequently, he was given monthly IV cyclophosphamide of 0.5g/m2 beginning at 3rd week of presentation for 5 doses to reach a total of 6 intravenous cyclophosphamide doses. Prednisolone was tapered to 10 mg a day. Serum creatinine further improved to 146 µmol/L over the following 6-month period.

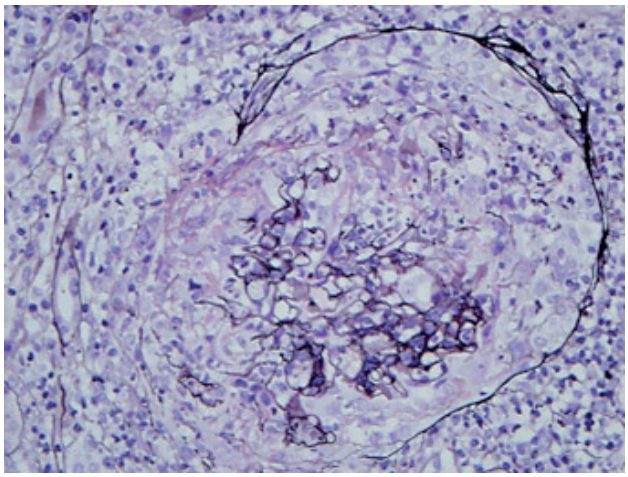

Figure 1: Methenamine silver x 400. A glomerulus with large cellular crescent and disruption of Bowman capsule

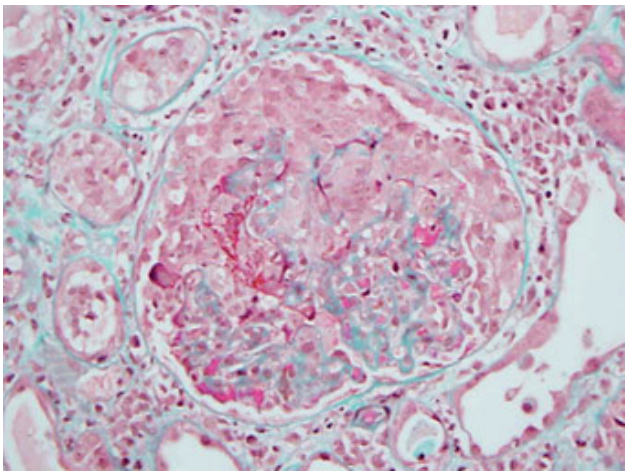

Figure 2: Masson trichrome x400. A glomerulus with fibrinoid necrosis and cellular crescent

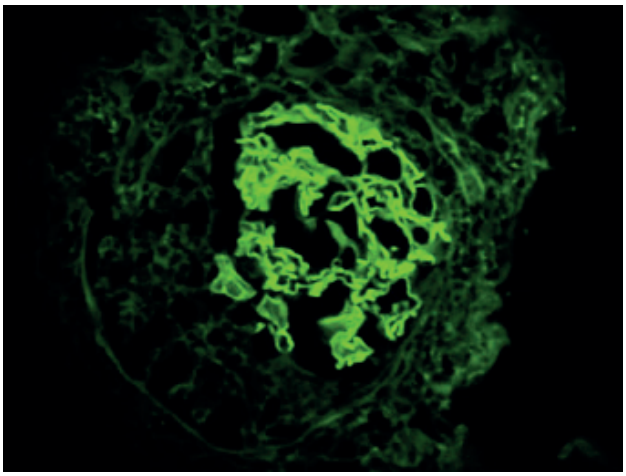

Figure 3: Immunofluorescent stain x400. Linear IgG positivity along the glomerular basement membrane

DISCUSSION

ANCA and anti-GBM are two antibody populations that are antigenically distinct (2). However, several case series reported that around fifty per cent of patients with the anti-GBM disease have the concurrence of circulating ANCA. This association is unknown. Suggested aetiology is the presence of ANCA causing glomerular injury and triggering the development of antiGBM antibodies by exposing the α-3(IV)NC1 antigen in the glomerular basement membrane (3). On light microscopy, 'Double-positive' disease often shows interstitial fibrosis, tubular atrophy and asynchronous crescents, which are the evidence of chronic injury compared to single positive anti-GBM disease, explaining the clinically longer prodrome of illness1. The finding of ANA positivity in this patient was unlikely to be significant given the patient do

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not achieve American College Rheumatology criteria for the diagnosis of Systemic Lupus Erythematosus (SLE).

Patients who have Double-Positive disease had an older age distribution similar to ANCA- associated glomerulonephritis which was 46 - 76 years old. In contrast, the age distribution is bimodal for patients with single positive anti-GBM disease. There is no significant difference in gender distribution for both diseases (1). It had been reported that patients who presented with dialysis-dependent renal failure secondary to Double-Positive disease have better renal survival at one year, which was 53 per cent compare to single positive anti-GBM disease, which was 44 per cent. It was also reported that 22 per cent of the patient with Double-Positive anti-GBM disease had relapse of their disease beyond 6 months follow up. No relapse of disease been reported for the patient with single positive anti-GBM disease. The median time of the first relapse for the patient who had double-positive disease was 4.4 years with a range of 1.1 to 7.9 years. Majority of these patients showed a rise in serum ANCA titres of more than 25% with the absence of serum anti-GBM antibodies. Therefore, maintenance immunosuppression therapies are mandatory for patients who have Double-Positive (1). To date, guidelines on the choices of immunosuppression therapies for patients with double-positive disease is not yet fully established. Several drugs like Azathioprine, Mycophenolate Mofetil, Cyclosporin had been tried with variable outcomes. In view of the possibility of relapse in double-positive disease, we planned to start this patient on azathioprine as the long-term maintenance immunosuppressive agent once the disease is in remission. The duration of maintenance immunosuppressive therapy will be at least 24 months.

Initial treatment of Double-Positive disease includes plasma exchange for 14 days or until serum anti-GBM antibody level is suppressed, combined with high dose steroid followed by oral cyclophosphamide at a dose of 2-3mg/kg daily for 3-6 months (4). Anticipating longer duration of immunosuppressive therapy after the initial 6 months because of the double-positive antibody status, we opted for IV cyclophosphamide 0.5 g/m2 monthly instead of oral cyclophosphamide to reduce the cumulative cyclophosphamide dose. Although no evidence as yet supports the use of IV, in preference of oral cyclophosphamide in double-positive disease, the marked improvement of renal function in our patient over the 6 months is encouraging. There is no proposed second-line agent for the initial treatment of the patient with the double-positive disease, only several case reports suggest that mycophenolate mofetil may be a reasonable option in the treatment of single positive anti-GBM disease (5).

CONCLUSION

Double-positive Anti-GBM and ANCA Associated Glomerulonephritis is a rare disease with better renal survival outcome in comparison with single positive Anti-GBM disease. However, the chance of relapse is higher in double-positive disease. IV cyclophosphamide could be a viable alternative to oral cyclophosphamide in such cases to reduce overall immunosuppressive load.

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