J Renal Inj Prev. 2018; 7(3): 211-214.

http://journalrip.com

DOI: 10.15171/jrip.2018.49

Journal of Renal Injury Prevention

Reversible personality changes caused by brain nocardiosis in a 74-year old Caucasian male renal transplant recipient following disease-specific antimicrobial therapy

Macaulay Amechi Onuigbo[1,2], Nneoma Agbasi[3]

[1]Mayo Clinic College of Medicine, Rochester, MN, USA
[2]Department of Nephrology, Mayo Clinic Health System, Eau Claire, WI, USA
[3]North East London NHS Foundation Trust, United Kingdom

ARTICLE INFO

Article Type:
Case Report

Article History:
Received: 8 November 2017
Accepted: 10 December 2017
Published online: 9 January 2018

Keywords:
Brain abscess
Brain nocardiosis
Immunosuppression
Pharmacovigilance
Renal transplant recipient

ABSTRACT

The management of potentially life-threatening brain nocardiosis in an elderly renal transplant recipient with the relevant specific antimicrobial agents while still continuing anti-rejection immunosuppressive therapy poses major clinical, pharmaceutical and logistical problems. This is a case of a 70-plus year old Caucasian male renal transplant recipient on maintenance immunosuppression, who developed a left flank abscess that was later complicated by the onset of personality changes from brain nocardiosis. The evolution of the diagnosis, treatment and recovery in this case presentation highlight the need for microbial susceptibility testing, the need for pharmacovigilance to monitor drug intolerance and drug resistance as well as other overarching treatment strategies including a close collaboration between Infectious Diseases and Transplant Medicine specialties in the management of this complicated case.

Case Report

Implication for health policy/practice/research/medical education:
A 74-year old Caucasian male renal transplant recipient on maintenance immunosuppression developed a left flank abscess that was later complicated by the onset of personality changes due to brain nocardiosis. The evolution of the diagnosis, treatment and recovery highlighted the need for microbial susceptibility testing, pharmacovigilance to monitor drug intolerance, drug toxicities and drug resistance. Such cases demand a very close and cooperative collaborative relationship between infectious diseases and transplant medicine specialties.

Please cite this paper as: Onuigbo MA, Agbasi N. Reversible personality changes caused by brain nocardiosis in a 74-year old Caucasian male renal transplant recipient following disease-specific antimicrobial therapy. J Renal Inj Prev. 2018;7(3):211-214. 10.15171/jrip.2018.49

Introduction

The management of potentially life-threatening brain nocardiosis in an elderly renal transplant recipient with the relevant specific antimicrobial agents while still continuing anti-rejection immunosuppressive therapy poses major clinical, pharmaceutical and logistical problems.

Case Report

A 74-year old Caucasian diabetic hypertensive male with a cadaveric renal allograft from 2011, on maintenance immunosuppression (Myfortic 540 mg/d, Prednisone 5 mg/d, tacrolimus 2 mg BID) developed a left flank abscess while spending the winter in Florida in February 2012. The abscess was drained and sent for appropriate cultures. He initially received oral cephalexin, which was then switched to IV vancomycin when gram positive organisms were identified. Subsequently, on suspicion for either nocardiosis or actinomycosis, and since the abscess had not improved, IV ceftriaxone was started.

***Corresponding author**: Macaulay Amechi Onuigbo, Email: onuigbo.macaulay@mayo.edu

The flank abscess improved and since the patient was to return up north to Wisconsin, he was switched to oral minocycline after 14 days of IV ceftriaxone. In early April 2012, back in Wisconsin, the wife noticed that the patient had developed new personality changes, was now more forgetful and "behaved strangely" like waking up at night and rummaging through his medicine bottles. The spouse secured his medications. We then evaluated him.

Other medical history included atrial fibrillation and hypothyroidism. Vital signs were stable. Chest and cardiac examination were unremarkable. Neck was supple. Abdominal examination revealed a nearly healed 3 cm left flank wound. He was awake, alert, non-focal, and appropriately oriented in person, place and time. He was intermittently forgetful and was irritable. Right sub-scleral hemorrhage was evident from a previous vitrectomy. Both pupils were equal and reactive to light and accommodation. Extra-ocular movements were full, corneal reflexes were present bilaterally, no facial asymmetry, tongue was in the midline, sensory and motor system examination was unremarkable, and deep tendon reflexes were normal in all four extremities. He however had an unsteady gait. There was no clonus or Babinski's sign, and cerebellar examination including finger-to-nose test was normal.

Laboratory evaluation showed the following: WBC 6.4 × 10^9/L, hemoglobin 12.3 g/dL, platelet count 189 × 10^9/L, serum creatinine 1.78 mg/dL (at baseline). Liver profile, TSH, dipstick urinalysis, urine cultures, and two sets of blood cultures, and also blood for CMV DNA by PCR were all normal or negative. Chest radiograph was unremarkable. Contrast-enhanced brain MRI showed multiple intracranial lesions, the largest was a bi-lobed mass in the right temporal area with surrounding edema (Figure 1A).

Brain abscess (nocardiosis) was empirically diagnosed, based on clinical suspicion (1-6). The dose of Myfortic was reduced by 50%. Initial empiric broad spectrum antibiotic treatment after specialty infectious disease consultation included IV meropenem 2 g every 12 hours, oral trimethoprim/sulfamethoxazole at 6 mg/kg/d trimethoprim given every 8 hours in three divided doses, and IV linezolid, 600 mg every 12 hours. The dose of trimethoprim/sulfamethoxazole was reduced after the first few days due to increasing creatinine to 3 mg/kg/d still in three divided doses. A week into the admission, the reference laboratory in Florida with the flank abscess specimen had identified the organism as *Nocardia* spp, by phenotypic identification in cultures. The antibiogram, as determined by the minimum inhibitory concentration (MIC) method using the microbroth dilution method, demonstrated resistance to trimethoprim/sulfa and imipenem. Trimethoprim/sulfa and meropenem were therefore discontinued. IV linezolid was continued, and IV ceftriaxone and IV amikacin were initiated. Linezolid was soon discontinued due to thrombocytopenia and leucopenia. Oral moxifloxacin 400 mg/d was substituted for linezolid. Gait and mentation improved. He was discharged after twelve days on IV amikacin 560 mg every 12 hours, IV ceftriaxone 2 g every 12 hours, and oral moxifloxacin 400 mg/d. With increasing serum creatinine, the dose of IV amikacin was reduced to 560 mg once daily. Serum creatinine continued to rise (2.6 mg/dL) and he developed persistent cough with wheezing. IV Amikacin was therefore discontinued. Cough with wheezing quickly resolved and the serum creatinine improved, once again. In October 2012, whilst on IV ceftriaxone and oral moxifloxacin, he developed severe generalized exfoliative dermatitis which rapidly resolved following the discontinuation of IV ceftriaxone. He completed 12 months of oral moxifloxacin 400 mg daily in April 2013. A follow up contrast-enhanced brain MRI from October 2013, after completing a total of over eighteen months of antimicrobial therapy, showed near clearance of the abscesses (Figure 1B). As at October 2014, the patient had remained otherwise asymptomatic nearly a year after completing the oral moxifloxacin course. He has continued to do well, off antifungals and has continued immunosuppression with Prednisone 5 mg daily, tacrolimus 1 mg every 12 hours (50% of original dose from April 2012), mycophenolic acid 360 mg in am, 180 mg in pm, and his current serum creatinine was 1.4 mg/dL as at August 2015. It is acknowledged that trimethoprim/sulfa was discontinued in April 2012 as a result of antibiotic resistance and was never restarted as his prophylactic transplant immunosuppression antibacterial regimen.

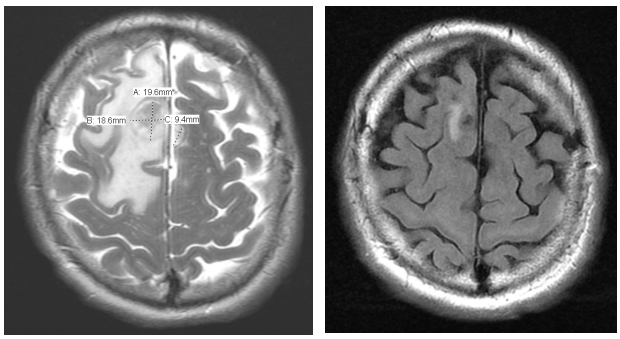

Figure 1. Composite figure showing brain MRI at diagnosis of Nocardia abscess (A) in April 2012 and repeat brain MRI (B) in October 2013 after 18 months of antimicrobial therapy.

The principle of antagonism between concurrently administered antimicrobials

One important consideration during his management was in reference to the possible antagonism between combination antibiotics in the treatment of nocardiosis in immunocompromised transplant recipients (7). This analysis demonstrated that whereas bactericidal synergism was observed for piperacillin/tazobactam combined with cotrimoxazole or moxifloxacin against 1 and 2 isolates, respectively, an antagonistic effect was seen for combinations containing linezolid (with amikacin

in 8 cases, with imipenem in 2, and with piperacillin/tazobactam in 1 case) and for the combination of piperacillin/tazobactam with amikacin in 1 isolate. All the other antibiotic combinations displayed indifferent activity. Because linezolid was discontinued early in the course of his treatment due to thrombocytopenia and leucopenia, we did not have to deal with this potential antibiotic-antibiotic antagonism involving linezolid.

Experiences with the management of adverse reactions to antimicrobials and the use of antibiogram sensitivities

Furthermore, the patient at various times exhibited a variety of adverse reactions to different antimicrobials and these therapeutic challenges were managed promptly and collaboratively with a very strong cooperative relationship between infectious diseases and transplantation medicine specialties. Moreover, we utilized results of culture sensitivity test results:

1. Worsening renal allograft acute kidney injury within days of initiation of oral trimethoprim/sulfa. The drug dose was initially reduced by 50% and kidney function stabilized.
2. Subsequently, following evidence of *Nocardia* spp. with drug-resistance to Imipenem and trimethoprim/sulfa, IV trimethoprim/sulfa and IV meropenem were discontinued. IV linezolid was continued, and IV ceftriaxone and IV amikacin were initiated.
3. The patient subsequently developed severe thrombocytopenia and leucopenia leading to the discontinuation of IV linezolid. Oral moxifloxacin 400 mg/d was substituted for linezolid.
4. Post-discharge from the hospital, he again developed acute kidney injury and the dose of IV amikacin was reduced by 50% to 560 mg once daily. Serum creatinine continued to rise (2.6 mg/dL), he developed persistent cough with wheezing so IV amikacin was therefore discontinued. Renal allograft function normalized and the cough and wheezing resolved.
5. Six months into antimicrobial therapy, in October 2012, whilst on IV ceftriaxone and oral moxifloxacin, he developed severe generalized exfoliative dermatitis which rapidly resolved following the discontinuation of IV ceftriaxone.

He subsequently was continued only on oral moxifloxacin for another 12 months to complete therapy of the brain nocardiosis.

Discussion

We have presented the intricate complexities involved in the management of symptomatic brain nocardiosis complicating immunosuppression from renal transplantation anti-rejection agents in a 70-plus year old Caucasian male patient. The potential for drug-drug interactions and other relevant adverse drug effects in combining chronic maintenance immunosuppression in an elderly patient while still aggressively treating a life-threatening nosocomial brain infection was highlighted. Such a case calls for a very strong, close and lasting collaborative effort between transplantation medicine and infectious diseases medicine specialties.

Post-script

The patient has continued to do well. In November 2016, the patient now 79 years old remains otherwise active as a retired Senior Citizen, with a serum creatinine of 1.5 mg/dL, hemoglobin 13.4 g/dL, WBC 6.5 × 10^3/μL and his normal personality. His current immunosuppression regimen is prednisone 5 mg daily, tacrolimus 1 mg every 12 hours and mycophenolic acid (Myfortic 180 mg oral delayed release tablet), two tablets in the morning, and one tablet in the evening, taken 12 hours apart.

Conclusion

The management of potentially life-threatening brain nocardiosis in an elderly renal transplant recipient with the relevant specific antimicrobial agents while still continuing anti-rejection immunosuppressive therapy poses major clinical, pharmaceutical and logistical problems. Such cases demand a very close and cooperative collaborative relationship between Infectious Diseases Medicine and Transplantation Medicine specialties.

Learning points

Solid organ transplant immunosuppression predisposes to nocardiosis.

Reduced immunosuppression should be discussed and may improve patient outcome.

Microbial identification and susceptibility testing are critical.

Prompt combination antimicrobials preferred for 6-12 months.

Pharmacovigilance is mandatory – drug-intolerance/adverse effects and drug-resistance.

Collaboration between Infectious Disease and Transplant-Medicine is paramount.

Surgical treatment of brain nocardiosis (abscess) is not always necessary.

Acknowledgements

This work is dedicated to the memory of a very dear friend, Ikechukwu Ojoko (Idejuogwugwu), who passed away back home in Port Harcourt, Nigeria, some years ago, after a reported brief illness. Idejuogwugwu, you are truly missed.

This work is also dedicated to the memories of the 153 Nigerians who died in a fiery plane crash in Lagos, Nigeria, on June 3, 2012. May their souls rest in perfect peace.

Finally, we dedicate this work to the memory of late Professor Dimitrios Oreopoulos. He was indeed a great teacher and mentor to the first author.

Authors' contribution

MAC: Conception, design, acquisition of data, data analysis, interpretation of data, literature review,

acquisition of data, literature review, drafting the article and final approval of manuscript. NA: Critical revising for important intellectual content, design, and final approval of manuscript.

Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patient has given his informed consent to publish this case report.

Funding/Support

None.

References

1. Eshraghi SS, Heidarzadeh S, Soodbakhsh A, Pourmand M, Ghasemi A, Gramishoar M, et al. Pulmonary nocardiosis associated with cerebral abscess successfully treated by co-trimoxazole: a case report. Folia Microbiol (Praha). 2014;59:277-81. doi: 10.1007/s12223-013-0298-7.
2. Lebeaux D, Morelon E, Suarez F, Lanternier F, Scemla A, Frange P, et al. Nocardiosis in transplant recipients. Eur J Clin Microbiol Infect Dis. 2014;33:689-702. doi: 10.1007/s10096-013-2015-5.
3. Wang HK, Sheng WH, Hung CC, Chen YC, Lee MH, Lin WS, et al. Clinical characteristics, microbiology, and outcomes for patients with lung and disseminated nocardiosis in a tertiary hospital. J Formos Med Assoc. 2015;114:742-9. doi: 10.1016/j.jfma.2013.07.017.
4. Minero MV, Marín M, Cercenado E, Rabada´n PM, Bouza E, Munoz P. Nocardiosis at the turn of the century. Medicine (Baltimore). 2009;88:250-61. doi: 10.1097/MD.0b013e3181afa1c8.
5. Flateau C, Jurado V, Lemaître N, Loïez C, Wallet F, Saiz-Jimenez C, et al. First case of cerebral abscess due to a novel *Nocardia* species in an immunocompromised patient. J Clin Microbiol. 2013;51:696-700. doi: 10.1128/JCM.00762-12.
6. Cassir N, Million M, Noudel R, Drancourt M, Brouqui P. Sulfonamide resistance in a disseminated infection caused by *Nocardia wallacei*: a case report. J Med Case Rep. 2013;7:103. doi: 10.1186/1752-1947-7-103.
7. Tripodi MF, Durante-Mangoni E, Fortunato R, Cuccurullo S, Mikami Y, Farina C, et al. In vitro activity of multiple antibiotic combinations against Nocardia: relationship with a short-term treatment strategy in heart transplant recipients with pulmonary nocardiosis. Transpl Infect Dis. 2011;13:335-43. doi: 10.1111/j.1399-3062.2010.00588.x.