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QATAR MEDICAL JOURNAL

CASE REPORT

Varicella-zoster virus associated encephalitis in a patient undergoing haemodialysis

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http://dx.doi.org/10.5339/qmj.2015.19
Submitted: 12 October 2015
Accepted: 12 January 2016

Cite this article as: Al-Mula Abed YW. Varicella-zoster virus associated encephalitis in a patient undergoing haemodialysis, Qatar Medical Journal 2015:19 http://dx.doi.org/10.5339/qmj.2015.19

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ABSTRACT

We describe an elderly gentleman with end stage renal disease on haemodialysis who presented with ophthalmic zoster infection and was discharged on oral acyclovir. He presented again a few days later with confusion and expressive dysphasia. Differential diagnosis was mainly between varicella-zoster virus (VZV) associated encephalitis versus acyclovir toxicity. Cerebrospinal fluid analysis confirmed the diagnosis of VZV associated encephalitis and the patient was treated with intravenous acyclovir and steroids with full recovery back to pre-admission neurological status.

Keywords: varicella zoster, encephalitis, haemodialysis, acyclovir toxicity

INTRODUCTION

Varicella-zoster virus (VZV) is a DNA virus and is a member of the herpes virus family. It has the capacity to persist in the body after primary infection (chicken pox). VZV reactivation is increasingly prevalent in immunosuppressed and elderly patients. It usually results in dermatomal cutaneous zoster known as shingles from the Latin *cingulum*, meaning belt.[1] Thoracic nerves and the ophthalmic division of the trigeminal nerve are the most commonly affected sites. The central nervous system is the most common extracutaneous site of involvement. This may manifest as cerebellar ataxia, aseptic meningitis, encephalitis, cranial nerve palsies, transverse myelitis, seizure or any other stroke mimics. Post herpetic neuralgia is a painful sequelae of VZV reactivation defined as pain persisting more than three months after the disappearance of the shingles. Cellular immunity is known to be affected in uremic patients more than humoral immunity and this is not corrected

by dialysis. VZV associated encephalitis has previously been reported in a few dialysis patients and here we report another patient who developed enecephalitis despite being on oral treatment.[2–5]

CASE REPORT

A 70-year-old gentleman presented with a three day history of right periorbital pain. He was known to have end stage renal disease of unknown cause for which he was on haemodialysis via a right internal jugular tunnelled catheter three times a week for the last two years. He was also known to have hepatitis C virus (HCV) genotype IV that was successfully eradicated a few years ago. He was still being regularly followed up by the hepatology team with no evidence of relapse or cirrhosis. The most recent HCV polymerase chain reaction (PCR) was not detectable and his most recent liver ultrasound was normal. He was not diabetic and he had no other significant past medical history apart from well controlled hypertension. Arteriovenous fistula creation was previously attempted but was unsuccessful. There was no history of recent travel or contact with anyone sick. His regular medications included irbesartan 150 mg once a day, amlodipine 5 mg once a day, simvastatin 20 mg once a day, alfacalcidol 0.25 microgram once a day and sevelamer 800 mg three times a day with meals. Clinical examination showed right periorbital vesicular rash compatible with herpes zoster ophthalmicus secondary to reactivation of VZV in the ophthalmic division of the trigeminal nerve.
The patient was discharged on a renal adjusted dose of oral acyclovir (800 mg twice a day). A few days later, he presented with a few hours history of confusion and expressive dysphasia started shortly post-dialysis. Meningeal signs were negative and there was no other focal neurological deficit. Vital observations were normal and the rest of the clinical examination was unremarkable with no stigmata of chronic liver disease. Blood tests showed normal white blood cell count and differential, normal platelets count, normal coagulation profile, normal liver function tests, normal bone profile and normal C-reactive protein. Chest X-ray was normal and a CT brain scan showed no intracranial bleed, space occupying lesion or other acute pathology. Differential diagnosis was between acyclovir toxicity, central VZV infection and acute stroke. A lumbar puncture was done and cerebrospinal fluid (CSF) analysis is summarized in Table 1.

Based on clinical suspicion and before obtaining the viral screen results, the patient was started on renal adjusted dose of intravenous (IV) acyclovir (5 mg/kg once a day) together with oral steroid (prednisolone 50 mg once a day). A magnetic resonance imaging scan of the brain was performed the following day and showed no acute pathology other than moderate background of chronic small vessels disease. Later on, CSF viral screen showed that VZV PCR was detected (the rest of the viral screen was negative). Retroviral antibodies screen was negative. The patient made a good recovery back to baseline neurological condition and was discharged home in a stable condition after two full weeks of the above treatment.

Table 1. CSF analysis.

Parameter	Result	Reference range
Appearance	Clear and colourless	
White blood cells	108/cmm	< 5/cmm
Differential	90% mononuclear cells 10% polymorphs	
Red blood cells	6/cmm	
Protein	0.84 g/l	0.15 – 0.45 g/l
Glucose	3 mmol/L	1.8 – 4.7 mmol/L
Gram stain	No organism seen	
Culture	No growth	
Cryptococcus antigen	Negative	
Acid Fast Bacilli	Auramine stain negative Culture negative	
Viral PCR screen	VZV DETECTED Herpes simplex virus and enterovirus not detected.	

DISCUSSION

There is a paucity of data on the incidence and nature of VZV neurological complications in patients with end stage renal disease undergoing dialysis, whether haemodialysis or peritoneal dialysis. The dermatological evidence of VZV reactivation can usually be seen a few days before or after the neurological manifestations. However, it may not be seen at all in a few cases especially in immunocompromised patients. It is a well-known fact that immunity; both innate and adaptive, is impaired in uremic patients, but for unknown reasons, viral infections seem to occur less commonly than bacterial infections despite relative lymphopenia and lymphocytes dysfunction.[6] Patients treated with long-term haemodialysis are at an increased risk of VZV compared with the general population.[7] VZV DNA detection by PCR is currently the gold standard test and is far more accurate than antibody measurement. It has specificity of more than 95% but sensitivity of only 30%.[8] Acyclovir is a very effective agent in treating VZV but it is excreted by the kidneys so dose adjustment is always needed. Neurological symptoms of acyclovir toxicity can mimic VZV associated encephalitis and should always be considered in the differential diagnosis in addition to acute stroke. Measuring acyclovir level is not common in clinical practice and haemodialysis may help in the treatment of acyclovir toxicity.

An important point in distinguishing acyclovir toxicity from other conditions is the temporal association between the symptoms and acycolvir administration. Acyclovir is poorly removed by peritoneal dialysis whereas it is estimated that 45% of the total amount of drug can be removed in a three hour haemodialysis session, though clinical improvement may lag behind drug removal.[9] Steroids are now highly recommended in VZV patients with large-vessel encephalitis.[10]

A single dose zoster vaccine is now available in a few developed countries with good efficacy and safety profile.[8] Our patient had no risk factors apart from end stage renal disease and advanced age.

CONCLUSION

We reported a haemodialysis patient with VZV associated encephalitis which was proven by CSF-VZV PCR detection. The main other differential diagnosis was acyclovir toxicity and acute stroke. There was no evidence of secondary bacterial infections. The patient made a good recovery back to baseline status following a two week course of IV acyclovir and steroid. This case is compatible with the current limited literature available, but our patient developed neurological symptoms despite being on oral acyclovir for cutaneous VZV. It is important for primary healthcare and emergency physicians to be aware of VZV complications, acyclovir toxicity and the need for dose adjustment in renal patients. We do believe that there is a need for consensus policies for zoster vaccination in dialysis patients.

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