CASE REPORT

Complicated urinary tract infection caused by *Corynebacterium urealyticum* – A pathogen that should not be forgotten

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SUMMARY

Although *Corynebacterium urealyticum* has rarely been isolated in diagnostic laboratories, this bacterium can be a significant uropathogen causing significant complications. It causes cystitis and alkaline encrusted cystitis, commonly involved in patients who need prolonged hospitalization and bladder catheterisation. We report here a case of a 19-year-old young man who was diagnosed with N-Methyl D-aspartate receptor (NMDAR) encephalitis that requires hospitalization for optimization of rehabilitation treatment in Hospital Kuala Lumpur, Malaysia. His urine culture isolated slow growing gram-positive pleomorphic rods subsequently identified as *C. urealyticum*. Based on the risk factors, the isolation of *C. urealyticum* could not be simply dismissed as contaminants. The patient was treated successfully with vancomycin for two weeks.

INTRODUCTION

Corynebacterium urealyticum is a recognised pathogen causing urinary tract infection (UTI). This bacterium is commonly seen in people with co-morbidities such as tumour and inflammation, and favour for colonization of urinary catheters that often lead to ascending infection of the bladder mucosa.[1] *C. urealyticum*, formerly known as *Corynebacterium* CDC group D2, is an opportunistic nosocomial pathogen frequently reported to cause cystitis, alkaline encrusted cystitis, pyelonephritis and encrusted pyelitis.[2] This organism had been implicated with human infections since 1935, when it was first discovered. To our knowledge, data on *C. urealyticum* as an uropathogen is limited in Malaysia. The bacterium has a diphtheroid morphology that grows slowly on the culture plates and therefore can be frequently disregarded in routine urine cultures. The identification process can be challenging as *C. urealyticum* has a strong ability to split urea, to distinguish itself from other nonlipophilic *Corynebacterium* species.[1,2] *C. urealyticum* is mostly resistant to a large number of antibiotics such as aminoglycosides and macrolides.[3] However, it is generally still susceptible to vancomycin and teicoplanin. Therefore, accurate identification and appropriate therapy may reduce the avoidable complications of the infection. We report here a case of complicated *C. urealyticum* UTI in a young gentleman as a platform to bridge the clinico-microbiological gap in the care of the patient.

CASE REPORT

A 19 years old young man was recently diagnosed with N-Methyl D-aspartate receptor (NMDAR) encephalitis at Hospital Kuala Lumpur, Malaysia that required hospitalization for optimization of rehabilitation treatment. He lost his bladder control and was put on continuous bladder catheterization (CBD). After two weeks of admission, his urine was noted to be cloudy and stained with blood. He did not have any fever or dysuria. Urine analysis and blood investigations showed features of UTI with alkaline urine (Table I). He went for kidney, ureter and bladder (KUB) ultrasound scan that showed mild right hydronephrosis with proximal hydroureter and thickening of the right ureter wall.

Grossly, the urine was turbid. The urine culture revealed pure growth of tiny colonies on blood agar (BA) and CLED agar after 24 hours incubation. No growth was seen on MacConkey agar. After 48 hours of incubation, the BA showed pure growth of small, pinpoint, whitish to translucent colonies with no haemolysis (Fig. 1). The colony count on CLED agar also revealed similar colony morphology with significant colony count of >25 colonies based on a filter paper method (>10^5 colony forming units per millilitre of urine). Gram stain of the colony revealed gram positive pleomorphic rods resembling diphtheroids (photo was not taken). Rapid urease test was positive. After 72 hours of incubation, enough colonies were available and the isolate was successfully identified as *C. urealyticum* by Vitek ANC (BioMerieux) with 99% confidence level.

Antibiotic susceptibility was performed, and the organism was susceptible to vancomycin but resistant to cotrimoxazole. The patient responded well to vancomycin and the treatment was given for two weeks. Repeat urine culture and sensitivity test showed no isolation of *C. urealyticum*. Ultrasound KUB was repeated following completion of treatment and results revealed that the resolution of the thickening of the right ureter wall. No calculi were seen.

DISCUSSION

C. urealyticum is rarely isolated in Malaysia therefore a high index of suspicions based on the clinical history is of paramount importance. Unfortunately, not all requests for urine culture and sensitivity are completed with significant

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Table I: Blood and urine investigations are suggestive of urinary tract infection

Blood investigations	Admission day	Day diagnosed for UTI
Total White Cell count (x 10^9)	7.5	14.4
Haemoglobulin (g/dL)	13.4	13.7
Platelet (x 10^9)	257	178
Urea (mmol/L)	3.9	10.0
Sodium, Na (mmol/L)	139	138
Potassium, K (mmol/L)	2.7	4.5
Creatinine (umol/L)	82	68
Total protein	70	104
Albumin	42	39
Alanine Transaminase	34	58
Alkaline Phosphatase	49	86
Urine FEME		
pH		9.0
Protein		4+
Leucocytes		3+
White blood cell		541/uL
Appearance		Turbid

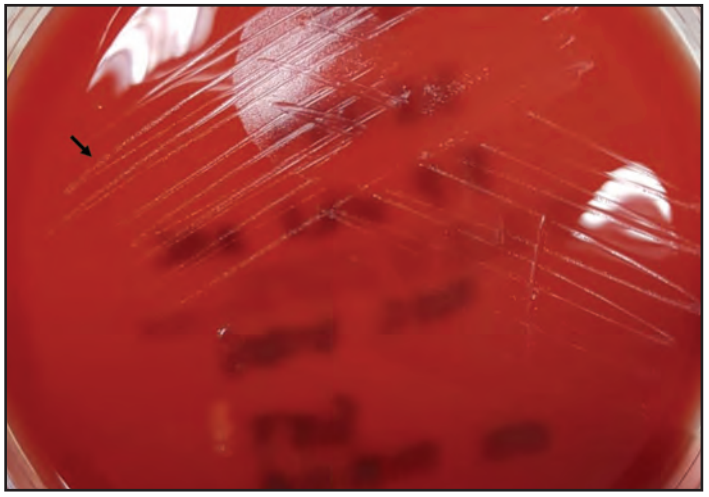

Fig. 1: Small, whitish to translucent pinpoint colonies (black arrow) of C. urealyticum on BA that can easily be regarded as contaminants after gram stain showed gram-positive pleomorphic rods resembling diphtheroids.

clinical history. Besides prolonged catheterisation and hospitalisation as observed in our patient, other risk factors for *C. urealyticum* infection include immunocompromised status, presence of chronic debilitating disease, recent urologic procedures, kidney transplant and usage of broad-spectrum antibiotics and cytotoxic drugs.[2] This pathogen can be easily missed in routine culture plate as the bacterium takes 48 hours to grow. In addition, the early appearance on the culture plate resembles a non-pathogenic colony; whitish, smooth, opaque and non-haemolytic.[4] Further consideration for investigations is needed when the gram stain of the colony shows gram positive pleomorphic rods and should not merely be regarded as skin contaminants or urethral flora.[2]

The urine FEME will show alkaline features that may have cellular casts or presence of struvite stones but these features are not specific to *C. urealyticum*. Another supportive test such as the urease test is needed. *C. urealyticum* is the only of the *Corynebacterium* species that displays the strongest urease activity.[1,2] This organism is also lipophilic and asaccharolytic, hence could be further differentiated as *C. urealyticum* from other *Corynebacterium* sp. by the production of acid from glucose except for *C. pseudodiphtheriticum*. The latter is an asaccharolytic organism but non-lipophilic and has weak urease activity 2. In addition to the biochemical test, Vitek ANC and API Coryne by BioMerieux are able to identify *C. urealyticum* correctly. Vitek ANC requires smaller inoculums compared to API Coryne that had enabled us to identify the colony correctly after 48 hours. Other parameters such as an increase in white cell count could signify an ongoing infection.

The pathogenicity of *C. urealyticum* is related to its strong urease activity. When the organism invades the uroepithelium, its growth is stimulated by the urea that is present in the urine.[1,2] The urea is hydrolysed, forming hyperammonuria and alkalinisation of urine. This condition leads to hypersaturation and favours for struvite and calcium phosphate crystallization. The crystal formation and its complications are best visualised by an ultrasound graph (USG) which was fortunately not present in our patient. This condition will lead to various clinical complications.

C. urealyticum is also a known multi-drug resistant organism (MDRO).[2,3] It mostly shows resistance to aminoglycosides due to the presence of *aph*(3′)-Ia gene that encodes aminoglycoside 3′-phosphotransferase [3]. This organism also has an *erm* (X) resistance gene that confers resistance towards macrolides [3]. Other antibiotic groups that have been increasingly reported for resistance include quinolones, chloramphenicol and tetracyclines. Vancomycin and teicoplanin are the main stay of treatment and have been shown to have great success in treating *C. urealyticum* UTI.[2] As this is a rare organism, no specific antibiotic susceptibility panel is available. Selected antibiotics were chosen following the consultation from our microbiologist, and the organism was tested susceptible to vancomycin and resistant to cotrimoxazole. The patient was successfully treated with intravenous vancomycin for two weeks.

Urinary tract infection caused by *C. urealyticum* is a nosocomial in origin as it is associated with prolonged catheterisation in our case. Good catheter care will reduce the recovery time from such infection.[2] Infection control measures have a special role in dealing with multi drug resistant organisms. These include standard precautions such as hand hygiene and contact precautions such as single room care patient and proper Personal Protective Equipment (PPE). These important measures will prevent the direct or indirect transmission of *C. urealyticum* when in contact with a patient or with the patient's environment.

CONCLUSION

C. urealyticum is a gram-positive rod that is easily missed in routine urine cultures as it takes 48 hours to grow, and it is commonly regarded as a contaminant or normal urethral flora. A high index of suspicion is warranted in patients with history of prolonged hospitalization and catheterisation, and this will help in isolating the pathogen. Thus, provision of a good clinical history to the laboratory is essential. *C. urealyticum* has a distinct strong urease activity and correctly identified by Vitek ANC. Prompt identification is vital as this is an MDRO and correct choice of antibiotic may prevent complications such as encrusted cystitis and recurrence. The treatment of choice is a course of vancomycin for two weeks. Good catheter care and strict infection control measure will increase the success rate of treatment and also prevent potential outbreak.

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