THE NEW ARMENIAN MEDICAL JOURNAL
Volume19 (2025), Issue 3, p.97-101

DOI: https://doi.org/10.56936/18290825-3.19v.2025-97

COVID-19 ASSOCIATED INCRUSTING CYSTITIS: A CASE REPORT

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Received 24.02.2024; Accepted for printing 15.05.2025

Abstract

On 11.03.2020, the World Health Organization declared the coronavirus disease (COVID-19) caused by the novel coronavirus (SARS CoV-2) a global pandemic. COVID-19 is a potentially severe respiratory infection caused by the SARS CoV-2 pathogen. SARS CoV-2 is an RNA-containing beta coronavirus. SARS-CoV-2 has a unique three-dimensional protein structure characterized by a strong binding affinity for angiotensin-converting enzyme 2 (ACE2) receptors. Under these conditions, human ACE2-producing organs may act as target cells for SARS-CoV-2.

Incrustation cystitis is believed to be a relatively rare complication in COVID-19 patients. The development of bladder lesions may be due to the disruption of blood flow to the bladder wall caused by SARS CoV-2. It is known that COVID-19 infection often causes hypercoagulation, which is accompanied by an increase in blood coagulation factors and endothelial dysfunction. Microcirculatory disturbances probably also play an important role in the pathogenesis of COVID-19-induced incrustation cystitis. The causes of hemodynamic disturbances are not fully understood and may be due to direct viral effects, immune-mediated mechanisms, or a combination of these. It is possible that bladder inflammation is caused by local endotheliitis, which is complicated by thrombosis of vessels of various calibers and increases ischemia of the bladder wall.

This case report of a 76-years-old woman who was hospitalized to the urology department complaining of painful, frequent urination, and blood in the urine. The case report describes the medical history, laboratory and instrumental examinations, surgical intervention, histological examination results, and follow-up of the patient.

Only urine acidification and endoscopic resection of the affected mucosa are considered effective in the treatment of encrusted cystitis. According to the literature, it is desirable that after resection, patients be treated with antibiotics against C. urealyticum. It has been established that C. urealyticum is sensitive to ofloxacin, norfloxacin and ciprofloxacin, fluoroquinolones, clinafloxacin, gemifloxacin, levofloxacin. Because newer antibiotics such as linezolid and quinupristin-dalfopristin have been shown to be effective in vitro against C. urealyticum strains, these antibiotics may prove to be useful alternative glycopeptides in the treatment of C. urealyticum infection caused by multidrug-resistant strains.

In conclusion in patients infected with Covid-19, with concomitant signs of urogenital tract infection, in addition to instrumental methods for detecting Incrustation cystitis, bacteriological studies were carried out to determine C. urealyticum. After endoscopic resection of the affected mucous membrane, it is advisable to choose a more targeted treatment tactic for C. urealyticum infection.

Cite This Article as:

Martirosyan D. A., Muradyan A. A. (2025). Covid-19 Associated Incrusting Cystitis: A Case Report; The New Armenian Medical Journal, vol.19 (3), 97-101; https://doi.org/10.56936/18290825-3.19v.2025-97

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Introduction

On 11.03.2020, the World Health Organization declared the coronavirus disease (COVID-19) caused by the novel coronavirus (SARS CoV-2) a global pandemic. As of August 6, 2023, there have been more than 769 million confirmed cases of the disease and more than 6.9 million deaths worldwide. Currently reported cases do not accurately represent the level of infection due to reduced testing and reporting worldwide. COVID-19 is now a recognized and ongoing public health problem. It continues to be one of the most important problems in modern medicine [*Zou X et al., 2020*]. Coronavirus disease (COVID-19) is a potentially severe respiratory infection caused by the SARS CoV-2 pathogen. SARS CoV-2 is an RNA-containing beta coronavirus. It is believed to have originated in bats, but the intermediate link between them and humans has not yet been identified [*Feng He et al., 2020*]. It is highly contagious, the main routes of transmission are contact and airborne. Aerosols containing the virus, which are produced by coughing or sneezing of infected people, are the main source of infection, and latent transmission can occur from asymptomatic patients [*Yongshi Yang et al., 2020*]. The incubation period for SARS-CoV-2 ranges from 2-14 days. COVID-19 is a disease that can have a mild or severe course of acute respiratory viral infection, may be accompanied by a number of other symptoms. The pathogenesis of the disease is characterized by the entry of viral particles into the lung endothelial cells by binding to the angiotensin-converting enzyme receptors, which leads to the development of a syndrome of activation of macrophages, natural killer cells, followed by a cytokine storm. A patient with COVID-19 usually has fever (98.6%), fatigue (69.6%), dry cough (59.4%), muscle pain (34.8%), shortness of breath (31.2%), as well as nausea and diarrhea (10.1%) [*Desouky E, 2021*]. The most common complication of the disease is bilateral viral pneumonia, which in many patients leads to respiratory failure. COVID-19 is multisystemic disease and can lead to damage to almost any organ in the body. The organs of the urinary system are no exception [*Lin L et al., 2020*]. SARS-CoV-2 has a unique three-dimensional protein structure characterized by a strong binding affinity for angiotensin-converting enzyme 2 (ACE2) receptors. Under these conditions, human ACE2-producing organs may act as target cells for SARS-CoV-2 [Ling Lin et al., 2020] Zhou and co-authors used a threshold of 1% ACE2-positive cells to identify organs at high risk of viral invasion and reported that the heart, spleen, esophagus, bladder (ACE2-positive cells in the bladder urothelium are 2.4%) and kidneys (ACE2-positive cells in the proximal tubules are 4%) may be target organs at high risk of viral invasion. This may explain the acute kidney injury that occurs in 0.1–29% of COVID-19 patients [*Xin Zou et al., 2020*].

Incrustation cystitis is believed to be a relatively rare complication in COVID-19 patients. Incrustation cystitis is a rare pathology, the main cause of which is a urinary tract infection, especially with urea-splitting bacteria [*Tarun J et al., 2022*].

C. urealyticum is a gram-positive bacterium that causes alkalinization of urine by degrading urea to ammonia, which in turn leads to the deposition of calcium phosphate and struvite in the bladder mucosa. The disease is characterized by calcification of the bladder mucosa, which can be diagnosed by instrumental examinations: ultrasound and CT scan, cystoscopy and biopsy. Urine acidification and endoscopic resection of mucosal lesions are effective in treating incrustation cystitis [*Puliatti S et al., , 2020*]. The development of bladder lesions may be due to the disruption of blood flow to the bladder wall caused by SARS CoV-2. It is known that COVID-19 infection often causes hypercoagulation, which is accompanied by an increase in blood coagulation factors and endothelial dysfunction. Microcirculatory disorders and ischemia of the bladder wall are a pathogenic factor and are found in many lower urinary tract pathologies [*Al Shukri S et al., 2011*]. Microcirculatory disturbances probably also play an important role in the pathogenesis of COVID-19-induced incrustation cystitis. The causes of hemodynamic disturbances are not fully understood and may be due to direct viral effects, immune-mediated mechanisms, or a combination of these. It is possible that bladder inflammation is caused by local endotheliitis, which is complicated by thrombosis of vessels of various calibers and increases ischemia of the bladder wall [*Varga Z et al., 2020*].

Case Report

A 76-year-old woman was hospitalized in the urology department, complaining of painful, frequent urination, and blood in the urine. The patient had been reporting the above complaints since January 2022, when uhe was hospitalized due to COVID-19 and had a urinary catheter. The patient did not mention any complaints or pathologies in the urinary system in her anamnesis. About 3 months before hospitalization, the patient had received treatment in the infectious disease department, where she was hospitalized with a diagnosis of COVID-19, interstitial pneumonia of bilateral viral etiology. During treatment, a urinary catheter was inserted, which was removed 10 days later. The patient received antibacterial, anti-inflammatory, hormonal, antiviral, anticoagulant, antihypertensive drugs, insulin and symptomatic therapy. In the urology department, a general urine test revealed 10-15 leukocytes and 2-4 erythrocytes in the field of view. A bacteriological test of urine performed twice did not show any growth of microorganisms, and mycobacterium tuberculosis was not detected. An ultrasound examination revealed thickening of the bladder walls, and a 2.4 *cm* formation was found on the right wall. An abdominal and pelvic CT scan with intravenous contrast was also performed, which revealed pathological thickening of the anterior and posterior walls of the bladder with incrustations. Taking into account the complaints and the results of instrumental examinations, cystoscopy was performed. During cystoscopy, the ureteral openings had a typical location, calcified and encrusted areas were visible over the entire surface of the bladder mucosa. Intact areas of the mucosa were present between the calcified, and encrusted areas of the bladder mucosa (white-arrows) (Fig. 1). An transurethral resection of the altered parts of the patient's bladder mucosa was performed, the removed tissue was sent for pathohistological examination (Fig. 2). After the operation, a urinary catheter was placed, an irrigation system was connected. The postoperative period was smooth, without complications, the irrigation system was removed on the second day after surgery, the urinary catheter was removed on the third day after surgery. The patient received appropriate antibacterial and anti-inflammatory therapy in the postoperative period. Pathohistological examination of the examined material revealed a picture of chronic, active cystitis with focal desquamation of the urothelium and foci of necrosis.

Seven months later, the patient was re-admitted to the urology department with the same complaints. A urine test revealed a significant number of erythrocytes in the urine. A bacteriological test of urine performed twice did not show any growth of microorganisms. An abdominal and pelvic CT scan with intravenous contrast was also performed, which revealed pathological thickening of the anterior walls of the bladder. Cystoscopy was performed, during which hyperemia of the bladder mucosa, slightly encrusted, altered areas of the mucosa were detected. This time also transurethral

Figure 1. *The patient was found to have focally altered, calcified (Выделено кругом), encrusted areas detected during cystoscopy.*

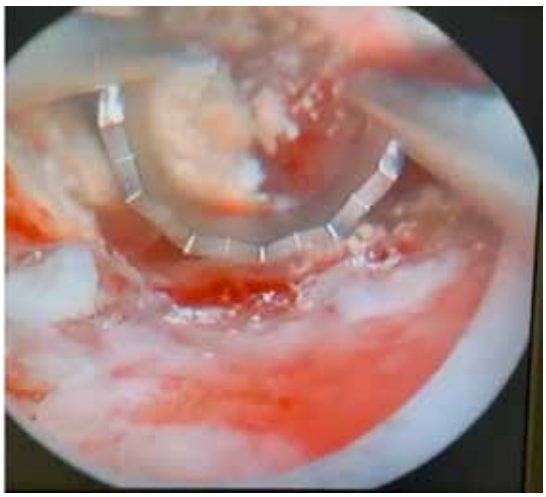

Figure 2. *Bladder after resection.The postoperative period was smooth, without complications.*

resection of the altered mucosa was performed, and the removed pieces were sent for pathohistological examination. Pathohistological examination of the examined material revealed the same picture of chronic, active cystitis with focal desquamation of the urothelium and foci of necrosis.

DISCUSSION

C. urealyticum is a gram-positive bacterium that causes alkalinization of urine by degrading urea to ammonia, which in turn leads to the deposition of calcium phosphate and struvite in the bladder mucosa. The disease is characterized by calcification of the bladder mucosa [*Puliatti S et al., 2020*].

The pattern of antimicrobial susceptibility of C. urealyticum varies among isolates obtained from different sources [*Nieto E et al., 2000*]. Most C. urealyticum strains obtained from clinical specimens typically exhibit multiple antibiotic resistance [*de Briel D et al.,1991, García-Rodríguez J et al.,1991, Funke G, Bernard KA, 2007*].

Considering the fact that the patient had signs of urological infection before admission to the infectious diseases department for treatment of COVID-19 infection and was subjected to antimicrobial treatment, and also that most strains of C. urealyticum obtained from clinical samples usually demonstrate multiple resistance to antibiotics, it can be assumed that the antibiotics taken did not affect the viability of C. urealyticum, which continued to calcify the bladder mucosa [*de Briel D et al., 1991, García-Rodríguez J et al., 1991, Funke G, Bernard KA, 2007*].

Based on this, only urine acidification and endoscopic resection of the affected mucosa are considered effective in the treatment of encrusted cystitis [*Puliatti S et al., 2020*], however, in our opinion, they are insufficient for the complete elimination of the disease. According to the literature, it is desirable that after resection, patients be treated with antibiotics against C. urealyticum. It has been established that C. urealyticum is sensitive to ofloxacin, norfloxacin and ciprofloxacin, fluoroquinolones, clinafloxacin, gemifloxacin, levofloxacin [*Santamaría M et al., 1985; Soriano F et al.,1987; Martínez-Martínez L et al., 2001; Sànchez Hernàndez J et al., 2003*]. Because newer antibiotics such as linezolid and quinupristin-dalfopristin have been shown to be effective in vitro against C. urealyticum strains, these antibiotics may prove to be useful alternative glycopeptides in the treatment of C. urealyticum infection caused by multidrug-resistant strains.

CONCLUSION

Thus, it can be concluded that in patients infected with Covid-19, with concomitant signs of urogenital tract infection, in addition to instrumental methods for detecting incrustation cystitis (calcification of the bladder mucosa), bacteriological studies were carried out to determine C. urealyticum. After endoscopic resection of the affected mucous membrane, it is advisable to choose a more targeted treatment tactic for C. urealyticum infection.

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THE NEW ARMENIAN MEDICAL JOURNAL
Volume19 (2025). Issue 3

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THE NEW ARMENIAN MEDICAL JOURNAL

Volume19 (2025). Issue 3

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Copy editor: Kristina D Matevosyan

LLC Print in "Monoprint" LLC

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