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Methicillin-Resistant Staphylococcus Aureus-Associated Colitis: Report Of An Emerging And Rare Infection

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Abstract
Most Cases Of Infectious Diarrhea Due To Staphylococcus Reported In The Literature Have Been Linked To A Risk Factor Such As Antibiotics. However, Since 1970, Cases Of Staphylococcus Aureus-Associated Enterocolitis Have Rarely Been Published. Here, We Report A Case Of A 42-Year-Old Man Who Had Acute Bloody Diarrhea Associated With Abdominal Pain And Altered General Condition. Radiological And Endoscopic Explorations Revealed Ulcerative Pancolitis And The Results Of The Stool Culture Were Positive For Methicillin-Resistant Staphylococcus Aureus (MRSA) And Negative For Clostridium Difficile. Empirical Antibiotic Therapy Was Initiated Including Ceftriaxone And Metronidazole And Then Replaced By Trimethoprim-Sulfamethoxazole After Antibiogram Results. In Terms Of Clinical, Biological, And Endoscopic Outcomes, The Evolution Was Satisfactory After Ten Days Of Treatment. The Occurrence Of MRSA-Associated Colitis Is Rare, Particularly In Patients Without Risk Factors For Infection. Thus, Whenever There Is Doubt, An Empirical Treatment Must Be Started Immediately After Collecting Stool Specimens For Coproculture..
Keywords: *Diarrhea, Methicillin-Resistant Staphylococcus Aureus, Infectious Colitis, Stool Culture*

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I. Introduction

Staphylococcus aureus-associated enterocolitiswas first described as an adverse event of antibiotics therapy or as an entity in antibiotics-naïve patients but having risk factors[1].However, until 1970, colonic infections were dominantly associated with *Staphylococcus aureus*which was recognized as the principal infective agent before its decline by the emergence of *Clostridium difficile*[1]. In addition to restricting a patient's hospital course, untreated methicillin-resistant *Staphylococcus aureus* (MRSA) associated colitis could also result in high mortality.In this paper, we report a case of rare colitis caused by MRSAin an adult patient without significant risk factors.To the best of our knowledge after our literature review, this case is the first to be reported in Morocco.

II. Case Presentation

Our patient was a 42-year-old man admitted for acute bloody diarrhea dating back 3 days at a rate of 5 to 8 stools per day which was associated with diffuse cramp-like abdominal pain. He also had intermittent nausea and vomiting with fever, chills, and significant asthenia. The personal history of our patient was marked by chronic tobacco smoking without any other familiar or personal diseases. The initial clinical examination found our patient slightly tachycardic (100 beats per minute), eupneic with 97% saturation, and subfebrile (37.9°C). He had minimal dehydration without pallor or mucocutaneous jaundice and his abdomen was tender.

Complete blood count and biomarkers showed an inflammatory syndrome that included high C Reactive Protein (CRP) at 100 mg/L, hyperleukocytosis (21000 elements/mm) with neutrophil dominance, anemia (hemoglobin at 11 g/dL), and normal ferritinemia (70 mg/L). Renal function and ionogram were both normal. A coproculture test with stool parasitology was also performed. An abdominal and pelvic computed tomography (CT) scan revealed a colonic wall thickening with a contrast agent enhancement, especially on the left which was characteristic of inflammatory or infectious colitis without signs of severity (**Figure 1**). and rectal and sigmoid endoscopy was also performed and showed an erythematous mucosa and localized congestive ulcerations of different sizes ranging from a few millimeters to 2 centimeters with intervals of healthy mucosa without endoscopic images of severity (**Figure 2**).

We initiated a dual empirical intravenous antibiotic therapy including ceftriaxone at a dose of 2g/day and metronidazole (500mg/8 hours) in combination with symptomatic treatment measures, namely rehydration, analgesics, and antispasmodics. Given the challenging diagnosis of infectious or inflammatory diseases,

treatment with corticosteroids was delayed. The evolution was marked by an improvement of clinical and biological symptoms on day 2 of antibiotic therapy.

A second endoscopic assessment under general anesthesia was performed and showed the same previously noticed lesions, this time extending to the cecum (**Figure 3**) with the last ileal loop of normal endoscopic appearance. The stool culture results were provided and were positive for *Staphylococcus aureus* and negative for *Clostridium difficile*. The antibiogram revealed resistance to methicillin, and intermediate sensitivity to ceftriaxone and quinolones but the germ was sensitive to other antibiotics. Oral treatment with trimethoprim-sulfamethoxazole at a dose of 160mg/800mg twice daily was initiated due to the shortage of vancomycin supply. The duration of treatment was ten days of trimethoprim-sulfamethoxazole and 14 days of ceftriaxone-based therapy in total with good clinical and digestive tolerance. Staged colonic biopsies were also performed during colonoscopy and showed non-specific colitis in particular ulcerative colitis or crhon's disease. The HIV test was negative. The follow-up after antibiotic treatment was marked by a complete resolution of the patient's complaints and symptoms. Biologically, CRP was negative after 7 days of treatment and a rectal and sigmoidoscopy performed on day 15 showed scar lesions on the mucosa. After 4 weeks, a total colonoscopy showed complete healing. Our patient returned to his professional activity at the end of the antibiotic therapy.

III. Discussion

Historically, *Staphylococcus aureus*was documented as the principal cause of post-antibiotic infectious diarrhea. Yet, after the publication of Barlett et al.'s report in 1978 which revealed *Clostridium difficile* as a major pathogen, very rare cases of *Staphylococcus aureus*-associated enterocolitiswere published in the medical literature [1]. These cases weremostly attributed to the recent use of antibiotics, chronic inflammatory bowel disease, or abdominopelvic surgery. Other risk factors have been reported in the literature and include long hospital stays (>72 hours), human immunodeficiency virus (HIV) infection, neutropenia, and nosocomial infections [1,2].Our patient had no mentioned previous risk factors. Diarrhea and vomiting were described in most published case series [7,8].The diagnosis was based on the use of coproculture. Co-infections of MRSA and *Clostridium difficile* are extremely rare and only two case reports were published to date [1].

The etiopathogenesis of *Staphylococcus aureus*-associated enterocolitisis primarily mediated by various toxins which explainsthe diversity ofitsglobal clinical picture. *Staphylococcus aureus* strains produceseveral toxins responsible for toxic shock. Importantly, staphylococcal enterotoxins and enterotoxins-like function as super-antigens which explains their high immunogenicity. It has been demonstrated that this notable toxic effect is associated with the presence of enterocytes that express toxin receptors and consequently, a direct action of these antigens on the cell, and on the other hand, to the activation of T lymphocytes associated with a cytotoxic storm affecting the structure and the functions of the enterocytes [3]. This is further supported by the presence of a biological infectious and inflammatory syndrome in all published cases.

The endoscopic spectrum of *Staphylococcus aureus*-associated enterocolitis is broad and also nonspecific. The use of colonoscopy was not performed in all published case series because of the risk of intestinal perforation. However, the available data on the described features include diffuse erythematous colitis, chronic necrotizing enterocolitis, pseudomembranous colitis, and severe pancolitis with multiple ulcerations [4]. Moreover, an appearance of rectal stenosis associated with massive colonic dilation and pancolitiswas also described [2]. Of note, a few cases of normal colonoscopy have also been reported[1].

Regarding the therapeutic management of this entity, vancomycin is still the antibiotic of choice. This first-line treatment is used in mostly all published case series. The duration varies between 10 and 14 days at a dose of 125 to 250 mg daily. However, it is recommended to use the sensitivity profile of the antibiogram of the isolated strain when selecting the optimal therapeutic approach. Daptomycin, metronidazole, quinolones, and doxycyclinecan also be used as a treatment either in a dual therapy in combination withvancomycinin case of sepsis andworsening of the general patient's conditions or as a second-line therapy after failure of vancomycin[1].Vancomycin and trimethoprim-sulfamethoxazole therapy combination can also be used in cases of MRSA-related colitis associated with ketoacidosis and complicated by appendicitis [5]. In our case, the use of trimethoprim-sulfamethoxazole provided a complete and satisfactory response, which is in line with the current knowledge supporting this antibiotics combination to treat *Staphylococcus aureus*-associated enterocolitis in patients without traditional risk factors [6].MRSA -associated colitis represents a rare etiology of infectious colitis, especially in patients who have no risk factors. In contrast to the literature, our observation remains different due to the absence of risk factors and the use of trimethoprim-sulfamethoxazole as an alternative to vancomycin, which can be a good option especially,forlow-income countries with vancomycin availability issues.

In conclusion, pseudomembranous colitis is commonly associated with *Clostridium difficile*which should be excluded first.When bacteriological specimens are taken for suspected infectious bacterial diarrhea, empirical broad-spectrum antibiotic therapy should be initiated.Before considering MRSAas the onlycause of

enterocolitis, other differential diagnoses of acute diarrhea must always be eliminated including other infectiousorganisms,ischemia, inflammatory conditions, and toxic or microscopic colitis.MRSA-producing endotoxins remain a significant etiology of infectious colitis, which must be systematically suspected in case of bloody diarrhea, especially in patients with risk factors.

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Figure Legends:

Figure 1. Abdominal and pelvic CT scan with an injection of contrast product in the portal phase showing colonic parietal thickening with contrast enhancement, especially on the left.

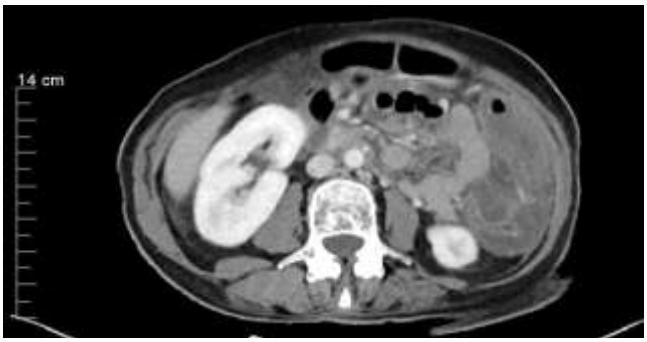

Figure 2 : . scattered ulcerations of different sizes with a whitish fibrinous background

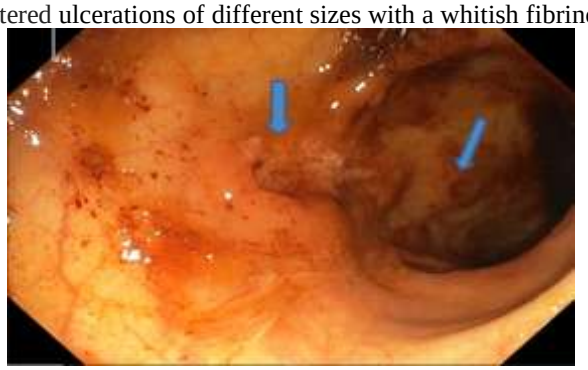

Figure 3 :scattered ulcerations of different sizes with a whitish fibrinous background extending from the rectum to the lower cecal fundus.