A case report of septic gardnerellosis

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ABSTRACT

Gardnerella vaginalis is a bacterium that is found as the most common cause of bacterial vaginitis in women. In this paper, we describe a case report of a 22-years old woman infected with G. vaginalis, who was initially suspected to have Dengue fever. The similarity of clinical symptoms developed by this disease with the symptoms of some other tropical infectious diseases, as well as a travel history, complicated identification of the disease cause for this particular patient. Here, we present a detailed epidemiological and clinical description of this case, leading to a final diagnosis of a septic form of gardnerellosis.

Introduction

Gardnerella vaginalis is a facultative anaerobic gram-negative bacterium that can be sexually transmitted from an infected partner, and can cause vaginitis [1]. Bacterial vaginosis is the clinical condition which results from a shift in the vaginal microbiota from Lactobacillus toward more diverse bacterial species, like Gardnerella [2]. Vaginitis is a more general term used to describe disorders of the vagina which are caused by inflammation, infection, or shifts in the normal vaginal flora; vaginitis can be caused by bacterial vaginosis, trichomoniasis, candida vulvovaginitis or diseases like chlamydia and gonorrhea [3]. Bacterial vaginitis is the most common genital disease in females of childbearing age, which leads to pelvic inflammatory diseases, endometritis, preterm births and spontaneous miscarriages in many cases [4]. Bacterial vaginitis is a polyetiological disease, and is caused by an imbalance of the vaginal microflora; in particular a decrease of Lactobacillus and an increase of anaerobic bacteria (e.g., G. vaginalis, Atopobium vaginae, Mobiluncus spp., Bacteroides spp. and Prevotella spp.) [5]. Frequently, vaginitis involves G. vaginalis infection [4,5].

The first demonstrated connection between G. vaginalis' and bacterial vaginitis was shown in 1955 [6]. At that time, G. vaginalis was believed to be the only etiological factor of vaginitis [7]. However, research conducted several years later determined that G. vaginalis was found in about 40 % of healthy females [5]. Further studies of the G. vaginalis genome in samples isolated from females with bacterial vaginitis identified two isolates with sequence identity averaging 93.62 %; however, only one of these two isolates were involved in the disease development [8].

Septic gardnerellosis affects patients of different age groups suffering from immunodeficiency, alcoholism and some chronic diseases such as diabetes, obesity, etc. [9,10]. Interestingly, no previous work to date has described the occurrence of septic gardnerellosis in immunocompetent individuals. In this paper we present a clinical case of an atypical course of septic gardnerellosis in a young healthy female with no signs of immunosuppression.

Case report

A 22-year-old woman, resident of Dnipro, Ukraine, was admitted for inpatient treatment at Lviv Oblast Infectious Clinical Hospital (LOICH) on day #9 of her illness. The patients anamnesis morbi detailed that the patient had been vacationing for two weeks in Bali, Indonesia. Disease onset was acute with cold chills and subfebrile temperature on the day #1 of the disease, which over the next two days rose to 39−40 °C. On day #3, a maculopapular rash appeared, accompanying the body temperature rise. The rash disappeared spontaneously every time the temperature normalized. Due to the rash eruption and fever, the patient visited the local hospital in Bali and received inpatient treatment for the next 48 h. Hemogram performed on day #3 of the disease reported the following results: hemoglobin (Hb) – 13.2 g/dL, red blood cells (RBC) – $4.66 \times 10^6/\mu L$, hematocrit (Ht) – 38.6 %, white blood cells (WBC) – $3.32 \times 10^3 /\mu L$, eosinophils – 0 %, basophils – 0.9 %, segmented neutrophils – 69.7 %, lymphocytes – 26 %, monocytes – 3.9 %, platelets – $117 \times 10^3/\mu L$. During the two days of hospitalization in Bali, the patient was prescribed intravenous drip infusion of

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5 % Glucose, 0,9 % NaCl. The patient was discharged from the hospital in Bali with a diagnosis of Dengue fever by day 3–4. This diagnosis was a clinical diagnosis and it is unknown whether the patient was tested for Dengue virus or other viral agents; therefore, a viral etiology could not be ascertained at that time for this patient. Following release from the hospital in Bali, the patient continued to display a fever (temperature 39–40 °C, showing no tendency to cycle within 24 h) and was administered paracetamol orally.

On day #7 post disease onset, the patient returned to Ukraine. She continued to present with a constant fever. Two days later (day #9), the patient was admitted to the LOICH with an initial diagnosis of Dengue fever. At admission, the patient's general status was evaluated as moderate with a temperature of 36.8 °C while treated with antipyretic drugs. During physical examination, the patient was alert, awake, and oriented and was able to answer the clinician's questions adequately. Her skin was pale and clean. The tongue was covered by a thin white layer. The posterior pharyngeal wall had a pink color; palatine tonsils mucous membrane and size were normal. Vesicular breathing was heard across the lung surface. Respiratory rate was 18 breaths per minute. The heartbeat sounded clear and regular, with a heart rate of 72 beats per minute. The abdomen was soft, nontender. Daily urine volume was sufficient, urine was straw-colored. The stool was formed one time per day. No meningeal signs or focal neurological symptoms were observed.

The hemogram at the admission at the LOICH on day #9 of disease showed: Hb – 13.2 g/dL, RBC – $4.76 \times 10^6/\mu L$, Ht – 38.6 %, WBC – $13.76 \times 10^3/\mu L$, neutrophils – 50.7 %, lymphocytes – 41.9 %, monocytes – 7.4 %, platelets – $348 \times 10^3/\mu L$, erythrocyte sedimentation rate (ESR) – 2 mm/h. A comprehensive metabolic panel was also obtained: total bilirubin – 12.2 μmol/L, alanine aminotransferase (ALT) – 302.5 U/L, aspartate transaminase (AST) – 181.5 U/L, creatinine – 65.8 μmol/L, urea – 2.83 mmol/L, amylase – 59.8 U/L, K^+ – 3.96 mmol/L, Na^+ – 142.0 mmol/L, Ca^{++} – 1.01 mmol/L. Since, the level of WBC, ESR and ALT was above the reference range, the admitting physician prescribed cefoperazone-sulbactam at 1 g b.i. d., glucose-saline solution intravenously and vitamin C to normalize the WBC count. While receiving this therapy, the patient continued to present with a fever.

The hemogram at day #11 of disease onset still showed abnormal results: Hb – 13.4 g/dL, RBC – $4.69 \times 10^6/\mu L$, WBC – $12.9 \times 10^3/\mu L$, neutrophils – 64.9 %, lymphocytes – 31.1 %, monocytes – 4.0 %, platelets – $465 \times 10^3/\mu L$, ESR – 24 mm/h. Urine analysis did not reveal significant changes. Biochemical blood analysis showed the following: total bilirubin – 14.2 μmol/L, ALT – 346.5U/L, thymol test – 11.4, creatinine – 78.4 μmol/L, urea – 5.3 mmol /L, glucose – 4.4 mmol/L, alkaline phosphatase – 4.2 μkat/L, cholesterol – 5.5 mmol/L, b-lipoproteins – 85.0 U; C-reactive protein (CRP) – 9 mg/mL (positive), anti-streptolisin-O (ASL(O)) – 63 IU/mL [Normal (N)<250 IU/mL], rheumatoid factor – 2 IU/mL (N < 6). Electrolytes level in blood was: K^+ – 4.78 mmol/L (N = 3,3−5,5 mmol/L), Na^+ – 134.0 mmol/L (N = 130−157 mmol/L), Ca^{++} – 1.18 mmol/L. A comprehensive analysis of blood clotting indicators showed no atypical results: prothrombin time – 19″ (N = 11−13″), prothrombin index – 79 % (N = 80−100 %), fibrinogen – 2.7 g/L (N = 2−4 g/L), hematocrit – 0.35 (N = 0.35−0.45).

Since the patient's vacation in Bali coincided in time with the beginning of the wet season there, at the Ukrainian hospital she was evaluated for mosquito-borne and other infectious diseases. Her blood samples tested negative for malaria (microscopic test), leptospira (microagglutination test), hepatitis virus (HBsAg and anti-HCV total in ELISA), Epstein-Barr virus (viral capsid antigen IgM in ELISA), cytomegalovirus (IgM in ELISA), HIV (cito-test) 1 and 2 types, *Salmonella typhi* (Widal's test) and *Treponema pallidum* (Wasserman reaction). *Streptococci viridans* was isolated from the

oropharyngeal swab on day #11 after the disease onset. Stool and urine cultures for pathogens of typhoid/paratyphoid group, dysenteric group and commensals were negative.

PCR tests for all 4 serotypes of the Dengue fever virus were negative for viral RNA. Similarly, PCR tests for Zika, West Nile, and Chikungunya viruses were also negative for viral RNA. ELISA testing and immunofluorescence assays for IgM and IgG to Dengue fever virus were negative. An ultrasound examination revealed an enlarged liver (the anterior-posterior dimension was 16.0 cm) and multiple hepatic hilar lymph nodes of up to 1.2 cm (size), and the spleen (14.5×6.5 cm). A chest X-ray and electrocardiography revealed no pathology.

During the disease course, while the patient remained on antibiotic therapy, fever remained steady, but with a slight downward trend with the maximum daily fluctuations up to 37.5–38.2 °C.

In the hemogram on day #13, leukocytosis and an increase in ESR were observed: Hb – 12.9 g/dL, RBC – $4.52 \times 10^6/\mu L$, WBC – $19.0 \times 10^3/\mu L$, granulocytes – 70.4 %, lymphocytes – 24.7 %, monocytes – 4.9 %, platelets – $473 \times 10^3/\mu L$, ESR – 32 mm/h.

On day #15, an echocardiogram was performed, which revealed no structural and functional changes in the heart valves. In addition, the patient was examined by a gynecologist on day #15, who established a provisional diagnosis of bacterial vaginosis - cervical dysplasia. A swab for flora and smear test for cytological screening was taken. The conducted clinical and laboratory tests (immunogram) did not reveal any immunodeficiency.

While on antibiotic therapy, the patient's health improved. On day #18 symptoms (rash, chills, hectic fever) and fever subsided. *G. vaginalis* was isolated from a blood sample taken on day 9 (admission to LOICH), using a Vitek 2 System 08.01 (Biomérieux, France). The isolated pathogen was sensitive to ciprofloxacin and levofloxacin.

The patient was discharged on day #21 of disease in satisfactory condition with normal indicators for CBC and blood chemistry results with the final diagnosis of septicemia, caused by *G. vaginalis*, severe course; vaginosis.

Discussion and conclusions

In the present study, we report a clinical case of septic gardnerellosis in an immunocompetent woman. This patient displayed abnormal WBC, ESR and ALT values and symptoms, including persistent, recurring fever, and rash. Laboratory and clinical results from the patient indicate systemic inflammatory response (SIRS): fever >38.0 °C or hypothermia <36.0 °C, tachycardia >90 beats/minute, tachypnea >20 breaths/minute, leucocytosis >$12*10^9$/l or leucopoenia <$4*10^9$/. Presence of two or more from these criteria is typical for SIRS, which is included in definition of sepsis [11,12]. Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection [13]. The diagnosis of bacterial vaginosis (BV) was based on the detection of the following symptoms (Amsel's criteria): presence of clue cells, vaginal ph greater than 4.5, positive whiff test, thin homogeneous vaginal discharge. Three of these symptoms must be present for a positive diagnosis according to Amsels criteria [14]. BV traditionally is determined as a noninflammatory syndrome without associated increased leukorrhea, but there are data which demonstrate the increased vaginal WBCs in females [15]. In these reports, proinflammatory indicators were also present. Additional research has described immune responses to gardnerellosis [16,17], as well as the effect of lysozyme, lactoferrin and β-defensin 2 on *G. vaginalis* virulence by comparing healthy females and those with BV [17]. However, while lysozyme was present, the effect was indistinguishable between isolates from the healthy and BV study groups.

Septic gardnerellosis is another form of the disease that has been associated with the isolation of *G. vaginalis* from the blood of women with postpartum endometriosis [18]. The incidence of preterm birth may also be affected by a bacterial vaginitis occurring in the early phase of pregnancy [19,20]. This pathogen may also be implicated in neonatal sepsis [21–23].

Additional reports describe the septic form of gardnerellosis occurring in infants [18], and in female and male immunocompromised patients [24,25]. Moreover, urinary abnormalities and alcoholism have shown to be contributing factors to *G. vaginalis* bacteremia in males and occasional cases of sepsis have been described [9,24,26–30].

It is worth mentioning that the diagnosis gardnerellosis in patients can be challenging as some clinical symptoms resemble those caused by many other infectious pathogens. Considering the epidemiological anamnesis and the patient's vacation in Bali [an endemic region for Dengue fever [31,32] the onset of the disease with fever and a rash on day 3, the diagnosis from the Indonesian hospital of Dengue fever is unsurprising (e.g., leucopenia and thrombocytopenia found in CBC results). However, we did not find that laboratory testing was performed to confirm or refute this diagnosis while the patient was in Bali, Indonesia. Upon return to Ukraine the fever continued, therefore the patient sought medical assistance at the LOICH.

It should be noted that Dengue fever is not endemic in Ukraine, but is rather exotic, so there are no approved treatment protocols for managing Dengue patients; thus, all information was taken from English-speaking sources during patient management at LOICH. Although the patient was admitted to LOICH with a fever (typical for Dengue), changes observed in the general blood analysis did not indicate Dengue fever infection, but rather suggested a bacterial infection (leukocytosis with increasing neutrophilosis). Therefore, the treating physician prescribed a broad spectrum antibiotic while the bacterial causative agent was being identified and the patient required immediate treatment. At the start of antibiotic treatment, blood and urine samples were taken from the patient. Additional laboratory tests on these samples identified gardennerella. However by the time the results were obtained the patient was recovering, likely due to the proactive prescription of the broad-spectrum antibiotic. Diagnostic tests performed on patient samples excluded relevant tropical viral or bacterial agents as the etiological agent (i.e., malaria, typhoid fever, Dengue, Zika, West Nile, and Chikungunya fever) and indicated that the patient displayed a septic case of *G. vaginalis* infection (*G. vaginalis* isolated from blood and urine samples).

To our knowledge, our study is a rare account of a case of *G. vaginalis* sepsis with the isolation of this causative agent from blood and vaginal secretion from a previously healthy, immuno-competent young woman.

Author statement

Eugenia Afi Datsomor – writing - original draft, investigation; Olena Zubach – writing - original draft, methodology, writing - review and editing; Nadiya Prykuda - writing - original draft, conceptualization; Alexander Zinchuk – supervision.

Compliance with ethics guidelines

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of Competing Interest

The authors declare they have no conflicts of interest.

Acknowledgments

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