Pneumonia Due to Mixed Infection From Atopobium Vaginae and Gardnerella Vaginalis Detected by Metagenomic Next-Generation Sequencing: A Case Report

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Case Report

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Abstract

Background

Atopobium vaginae and *Gardnerella vaginalis* are commensal vaginal bacteria. They are common pathogens of bacterial vaginosis and rarely cause pneumonia.

Methods

We report a case of a 27-year-old female with severe pneumonia, diabetic ketoacidosis, and hyperthyroidism. Notably, a mixed infection from *A. vaginae* and *G. vaginalis* was confirmed by metagenomic next-generation sequencing (mNGS).

Results

The mNGS of bronchoalveolar lavage fluid showed a total of 10,548 reads of *A. vaginae*, with a genome coverage rate of 26.63% and 5,237 reads of *G. vaginalis*, with a genome coverage rate of 34.76%. The patient recovered after ceftriaxone and ornidazole treatments.

Conclusion

This case demonstrated the advantage of mNGS in detecting unusual pathogens in pneumonia. Our diagnostic and treatment approaches could provide a reference for the future management of pneumonia due to a mixed infection from *A. vaginae* and *G. vaginalis*.

Introduction

Atopobium vaginae and *Gardnerella vaginalis* are commensal vaginal bacteria and the most common pathogens of bacterial vaginosis [1]. They rarely cause serious infections outside the genitourinary tract; only a case of severe peritonitis from the two bacteria following total hysterectomy with adnexectomy and a case of ventilator-associated pneumonia from *G. vaginalis* have been reported [2–3]. Due to its rarity and difficulty in bacterial detection and culture, the extra-genitourinary infection from these two bacteria can be easily misdiagnosed, which leads to delayed management and serious outcomes. Here, we report a case of a 27-year-old female with severe pneumonia, diabetic ketoacidosis, and hyperthyroidism. A mixed infection from *A. vaginae* and *G. vaginalis* was finally confirmed by metagenomic next-generation sequencing (mNGS) and successfully treated with ceftriaxone and ornidazole.

Case Presentation

A 27-year-old female was admitted to the hospital on January 26, 2022, with the chief complaints of fever, chest tightness, and shortness of breath for seven days, which exacerbated for four days. Seven days before her admission to our hospital, she started to develop fever and chills without any obvious cause. Her highest temperature was 38.6°C. In addition, she also had chest tightness and shortness of breath, profuse sweating, a maximum heart rate of 150 beats/min. Later on, she started to have a productive cough with a small amount of gray and thin mucus. Her past medical history included type II diabetes mellitus and hyperthyroidism, which was being treated with insulin, methimazole, and propranolol. The patient initially went to a local hospital on January 22. She received endotracheal intubation and mechanical ventilation due to hypoxemia and was admitted into the intensive care unit (ICU). She had no improvement in the next four days and was then transferred to our hospital. During the admission to our hospital, her temperature, heart rate, respiration rate, and blood pressure (vital signs) were 39.5°C, 188 beats/min, 26 beats/min, and 134/80 mmHg. She was awake but looked lethargic and had labored breathing and coarse bilateral breath sounds without obvious rales or crackles. Laboratory tests measured the white blood cells (11.8×10^9/L), neutrophils (8.0×10^9/L), C-reactive protein (72.6 mg/L), procalcitonin (6.1 ng/mL), blood glucose (34.0 mmol/L), hemoglobin A1C (13%), free triiodothyronine (5.8 pmol/L), free thyroxine (25.3 pmol/L), thyroid-stimulating hormone (< 0.005 mIU/L), blood gas analysis (FiO_2 50%) pH (6.95), $PaCO_2$ (26 mmHg), PaO_2 (184 mmHg), sodium (145 mmol/L), potassium (3.3 mmol/L), base excess (− 26 mmol/L), HCO_3 (− 5.8 mmol/L), and lactate (0.6 mmol/L). A urinalysis showed urine ketone 3+, occult blood 3+, protein 2+, and glucose 3+. A computerized chest tomography (CT) scan showed multiple patchy high-density shadows in the bilateral lungs, predominantly in the upper lobes with subpleural distributions (Fig. 1A–C). At admission, she was diagnosed with pneumonia, diabetic ketoacidosis, and hyperthyroidism. She received ceftizoxime and moxifloxacin as the anti-infective treatment, as well as hydration, antihyperglycemic, anti-thyroid, and electrolyte correction managements.

The sputum from the patient was sent for bacterial culture, which reported *Burkholderia cepacian* and *Candida glabrata*. The blood culture had no bacterial growth. The 1,3-β-D-glucan was < 10 pg/mL. The bronchoalveolar lavage fluid was sent for mNGS, which reported *A. vaginae* (10,548 reads, genome coverage rate 26.63%) and *G. vaginalis* (5,237 reads, genome coverage rate 34.76%) infection (Fig. 2). The mNGS of the blood sample was negative.

The patient was interviewed again. She reported a recent history of increased vaginal discharge with odor for more than one year without treatment. She was in a monogamous relationship and frequently washed her underwear together with other clothing. There was no intrauterine device (IUD) placement. Both *A. vaginae* and *G. vaginalis* are commensal vaginal bacteria. The pelvic examination was planned but canceled since she was on her menses. The anti-infective treatment was switched to ceftriaxone 4 g daily combined with ornidazole 0.5 g every 12 h. Her clinical symptoms improved, and the temperature decreased to about 38°C. On January 29, laboratory tests showed white blood cell counts, neutrophil counts, and procalcitonin levels of 6.9×10^9/L, 5.5×10^9/L, and 1.4 ng/mL, respectively. CT scan showed multiple patchy shadows in the bilateral lungs, predominantly in the upper lobes, and bilateral pleural

effusions with poorly expanded lungs. There were also increased fluid accumulations in the abdominal and pelvic cavities (Fig. 1D–F). A paracentesis was performed with 2,000 ml of yellow transudate drained. The ascitic fluid culture was negative. On January 30, she was extubated after her condition was stable and she was fully awake and alert. The pelvic examination was done, and the vaginal secretion was obtained three days after her menses was completed. The culture revealed the presence of *Escherichia coli* and *Enterococcus faecalis*. After treatments, her temperature returned to normal, with no more productive cough. On February 7, laboratory test showed white blood cell and neutrophil counts of 7.7×10^9/L and 6.2×10^9/L, and procalcitonin levels of 0.07 ng/mL. CT scan showed a few linear and patchy shadows in the bilateral lower lungs. Compared with the previous CT scans, most of the patchy shadows in both lungs disappeared, with only a small amount of pleural effusion on both sides (Fig. 1G–I). The abdominal and pelvic fluids also disappeared. The dynamic changes of the laboratory test results are presented in Table 1.

Table 1
The laboratory data of this case are presented in the form of timeline.

	Day 1	Day 3	Day 5	Day 8	Day 14
Infection					
White blood cell count, ×10^9/L	11.78	10.19	6.55	6.59	6.22
Neutrophil count, ×10^9/L	7.95	8.15	5.4	4.9	4.36
Neutrophil percentage, %	67.5	80	82.4	74.4	70.1
Procalcitonin, ng/ml	6.08	3.55	0.563	0.073	0.058
Organ function					
Alanine aminotransferase, U/L	83.6	52	29	27.3	11.4
Aspartate aminotransferase, U/L	88.3	34.6	17.6	37.4	9.7
Urea nitrogen, mmol/L	8.12	14.58	17.17	6.96	4.14
Serum creatinine, μmol/L	95.3	184.6	121.2	35.6	23.5
Troponin T, ng/L	56.5	47.36	30.31	29.28	17.72
Brain natriuretic peptide, pg/ml	6286	1742	1988	2997	160
Thyroid function					
Free triiodothyronine, pmol/L	5.82		2.54		6.51
Free thyroxine, pmol/L	25.26		14.83		27.19
Thyrotropic hormone, mIU/L	< 0.005		0.007		0.005

Discussion

Both *A. vaginae* and *G. vaginalis* are anaerobic and commensal bacteria in the female vagina. However, the microbiota can be altered due to various factors, including hormonal changes, sexually transmitted infections, IUD replacement, antimicrobial treatments, stress, and smoking. Glycogen can be used to synthesize biogenic amines that reduce the activity of the lactic acid bacteria. This can lead to the alkalization of the vaginal environment with accelerated bacterial growth, which finally causes bacterial vaginosis [4]. The pathogen is difficult to diagnose by the routine culture methods. A special culture medium, such as blood agar or chocolate agar medium, is required to grow the bacteria in an anaerobic environment.

mNGS can evaluate the entire nucleic acid sequences in a specific specimen with high sensitivity. This technology has made great progress in clinical pathogenic microbial diagnosis and has been increasingly used [5]. Xie et al. retrospectively studied the mNGS and conventional testing results in 140 patients hospitalized with suspected pneumonia [6]. They found that the positive detection rate of pathogenic bacteria was significantly higher with mNGS compared with the conventional tests (82.14% vs. 35.71%, $P < 0.05$). Patients with positive mNGS results had a significantly higher bacterial detection rate than patients with positive conventional test results ($P < 0.05$). The difference between 15 diabetic patients with infection (22.70%) and four patients with infection alone (7.84%) was statistically significant ($P = 0.03$), which suggested a high diagnostic advantage of mNGS for pneumonia, especially complicated pneumonia. Due to the unbiased and ultra-sensitive characteristics of the mNGS test, the sequencing results can be matched to various bacteria. This requires a comprehensive analysis and interpretation based on the bacterial species, sequence reads, suspected pathogens, and clinical characteristics to determine whether the microorganisms are commensal or pathogenic [7]. Our patient had symptoms of respiratory tract infection, a chest CT imaging with atypical bacterial infection with patchy infiltrations in the subpleural spaces in the bilateral upper lobes, and genitourinary commensal bacteria in the bronchoalveolar lavage fluid specimen. We thus believed that the pneumonia was due to a mixed infection from *A. vaginae* and *G. vaginalis*. Our patient had a history of type II diabetes and hyperthyroidism and a long-term history of bacterial vaginosis without standard treatment. These could be risk factors for serious wide-spreading infections when the immune function is decreased, especially if combined with poor personal hygiene habits.

It is well known that the recommended treatments for bacterial vaginosis are metronidazole/tinidazole and clindamycin. However, the recurrence rates in the medium and long-term follow-ups were high, regardless of the success of the initial treatment. This might be due to the antibiotic resistance of the vaginal pathogenic microorganisms [8]. There is no recommendation on the optional treatment regimen for pneumonia from *A. vaginae* and *G. vaginalis*, due to the rare incidence of these infections. There were reports to use piperacillin–tazobactam to successfully treat peritonitis from *A. vaginae* and *G. vaginalis* after total hysterectomy with adnexectomy and ceftriaxone to treat pneumonia from *G. vaginalis* [2, 9]. In the present patient, we gave ceftriaxone combined with ornidazole to treat her pneumonia from *A. vaginae* and *G. vaginalis* and achieved satisfactory outcomes.

We did not detect *A. vaginae* and *G. vaginalis* in the vaginal specimen in our patient. This might be due to the delayed pelvic examination and vaginal specimen collection since the patient was in menses at the beginning of hospitalization. The antibiotic treatment targeting *A. vaginae* and *G. vaginalis* might have caused the negative findings in the vaginal specimen collected after her menses.

Conclusion

To our knowledge, this is the first case report of severe pneumonia due to a mixed infection from *A. vaginae* and *G. vaginalis*. Our case presentation highlighted the advantage of mNGS in detecting unusual pathogens and reports a successful treatment.

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. Since no human experimentation was performed, no approval by an ethics board was required.

Consent for publication

The written informed consent for publication was obtained from the patient.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors have no conflicts of interest to declare.

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None.

Authors' contributions

Suming Zhou collected the clinical sample and data. Wenying Xia performed microbiological tests on the specimens. Qian Zhang and Yi Han constructed the manuscript. All authors read and approved the final manuscript.

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References

1. Onderdonk AB, Delaney ML, Fichorova RN. The Human Microbiome during Bacterial Vaginosis. Clin Microbiol Rev. 2016 Apr; 29(2):223–38.
2. Taillandier P, Roingeard C, Violette J, Leclère FM, Faivre S. **Septic shock caused by Gardnerella vaginalis and Atopobium vaginae**. **IDCases**. **2020 Jun 18;21**:**e00876**.
3. Ait Tamlihat Y, Augereau PF, Lardillon G, Violette J. Gardnerella vaginalis Is a Rare Cause of Ventilator-Associated Pneumonia: A Case Report and Literature Review. J Med Cases. 2021 Apr; 12(4):134–137.
4. Castro J, Rosca AS, Cools P, Vaneechoutte M, Cerca N. Gardnerella vaginalis Enhances Atopobium vaginae Viability in an in vitro Model. Front Cell Infect Microbiol. 2020 Mar 4; 10: 83.
5. Besser J, Carleton HA, Gerner-Smidt P, Lindsey RL, Trees E. Next-generation sequencing technologies and their application to the study and control of bacterial infections. Clin Microbiol Infect. 2018 Apr; 24(4): 335–341.
6. Xie G, Zhao B, Wang X, Bao L, Xu Y, Ren X, Ji J, He T, Zhao H. Exploring the Clinical Utility of Metagenomic Next-Generation Sequencing in the Diagnosis of Pulmonary Infection. Infect Dis Ther. 2021 Sep;10(3):1419–1435.
7. Simner PJ, Miller S, Carroll KC. Understanding the Promises and Hurdles of Metagenomic Next-Generation Sequencing as a Diagnostic Tool for Infectious Diseases. Clin Infect Dis. 2018 Feb 10; 66(5): 778–788.
8. Verstraelen H, Swidsinski A. The biofilm in bacterial vaginosis: implications for epidemiology, diagnosis and treatment: 2018 update. Curr Opin Infect Dis. 2019 Feb; 32(1): 38–42.
9. Bittar JM, Gazzetta J. Gardnerella vaginalis causing pulmonary infection in a young adult: A novel case. Respir Med Case Rep. 2019 Jul 25; 28: 100916.

Figures

Figure 1

See image above for figure legend

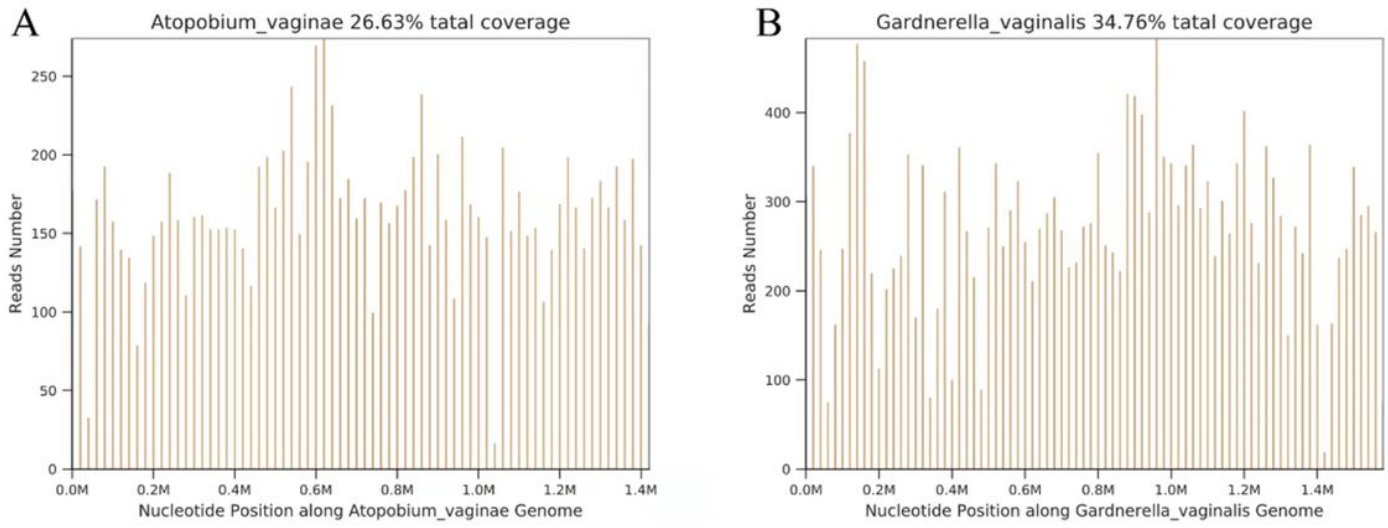

Figure 2. Metagenome second generation sequencing (mNGS) of bronchoalveolar lavage fluid (BALF) results for the patient. The identified sequence reads corresponding to *Atopobium vaginae* and *Gardnerella vaginalis* were10548, and 5237; with a genomic coverage of 26.63% (A) and 34.76% (B), respectively.

Figure 2

See image above for figure legend