



A rare case of adrenal gland abscess due to anaerobes detected by metagenomic next-generation sequencing

Wenting Jin¹, Qing Miao¹, Mengran Wang¹, Yao Zhang¹, Yuyan Ma¹, Yingnan Huang¹, Honglong Wu³, Yang Lin⁴, Bijie Hu^{1,2}, Jue Pan¹

¹Department of Infectious Diseases, Zhongshan Hospital, Fudan University, Shanghai 200032, China; ²Department of Infectious Diseases and Department of Infection Control, Zhongshan Hospital, Fudan University, Shanghai 200032, China; ³Binhai Genomics Institute, Tianjin Translational Genomics Center, BGI-Tianjin, BGI-Shenzhen, Tianjin 300308, China; ⁴BGI Genomics BGI-Shenzhen, Shenzhen 518083, China
Correspondence to: Jue Pan, MD. Department of Infectious Diseases, Zhongshan Hospital, Fudan University, 180 Fenglin Road, Shanghai 200032, China. Email: pan.jue@zs-hospital.sh.cn.

Abstract: A 50-year-old woman presented with right back pain, low fever, leukocytosis, a high level of C-reactive protein and a high erythrocyte sedimentation rate. Abdominal magnetic resonance imaging (MRI) revealed a hypodense lesion in the right suprarenal region, while PET/CT showed mildly increased metabolic activity. A CT-guided percutaneous puncture was performed, and foul-smelling thick pus was removed, which indicated an anaerobic infection. A smear of the pus showed both gram-positive and gram-negative microorganisms. Traditional culture only detected *Escherichia coli*, *Proteus mirabilis*, and *Actinomyces turicensis*. While surprisingly, metagenomic next-generation sequencing (mNGS) of both the pus and blood showed high reads of multiple pathogens, including anaerobes and the three culture-positive pathogens. Thus, adrenal gland abscess was confirmed, and a combination therapy of catheter drainage and effective antimicrobial treatment was started. Six days later, the patient had clinically improved and mNGS showed dramatically decreased reads of all pathogens. A follow-up lab examination of inflammatory biomarkers was normal, and the adrenal mass was reduced radiographically.

Keywords: Adrenal gland abscess; anaerobes; metagenomic next-generation sequencing (mNGS)

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Introduction

Adrenal gland abscess is rare in adults but less uncommon in newborns (1). It usually occurs in patients with conditions such as immunosuppression, HIV infection, or recent surgical procedures. Adrenal gland infection can develop through either the dissemination of a bloodstream infection or previous extravasated blood in the adrenal gland, which is more common. *Staphylococcus aureus* and *Escherichia coli* are the most common pathogens according to the literature (2), and *Streptococcus*, *Salmonella*, *Bacteroides*, *Echovirus*, *Herpes simplex virus*, *Cytomegalovirus*, *Nocardia*, *Tuberculosis*, fungi and parasites have also been reported (3-6). Here, we report a case of adrenal gland abscess caused by multiple pathogens, predominantly mixed anaerobes, identified via metagenomic

next-generation sequencing (mNGS) and culturing of *Escherichia coli*, *Proteus mirabilis* and *Actinomyces turicensis*. Next-generation sequencing technology identified specific nucleotides of the microbes in the samples and compared them to a DNA library through DNA fragmentation, end-repair, adapter-ligation and PCR amplification to identify possible pathogens in sterile areas (7-9). This technique is marked by its rapid diagnostic value and the advantage of simultaneously identifying multiple pathogens.

Case presentation

A 50-year-old previously healthy woman complained of right back pain and a low-grade fever of a 10-day duration. A previous abdominal CT scan showed a 7 cm-sized mass

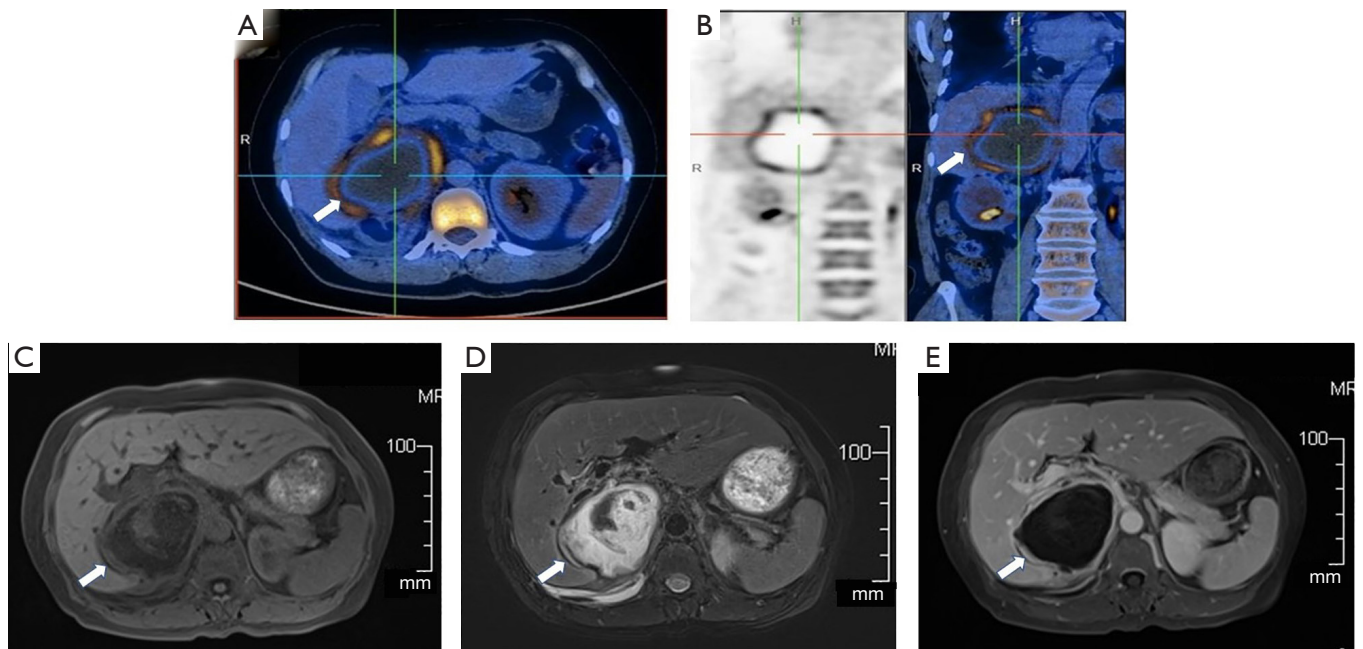


Figure 1 PET/CT and abdomen magnetic resonance imaging. (A,B) Revealed a hypodense lesion in the right suprarenal region (arrows) with mild elevated SUVmax 6.7. (C,D,E) Showed right adrenal mass (arrows) with a thick wall and inhomogeneous signal inside. (C) T1-weighted image on admission; (D) T2-weighted image on admission; (E) T1-weighted image with contrast on admission.

with a well-defined, thick wall, and laboratory testing showed leukocytosis (WBC count of 13,900 cells/mL) and an elevated C-reactive protein (CRP) level of over 90 mg/L. No improvement in symptoms occurred after the woman was prescribed ceftizoxime and metronidazole. For the further evaluation of malignancy, she underwent PET/CT scans, which revealed a hypodense lesion in the right suprarenal region with elevated SUV (6.7 for maximum). (Figures 1A,B) For further diagnosis, she was referred to the Department of Infectious Diseases, Zhongshan Hospital, Fudan University on 16th May, 2018.

Continuous worsening back pain without fever was found at admission, and the physical examination showed percussion pain on her right back. Admission labs showed leukocytosis (WBC count of 12,130 cells/mL) with elevated CRP (174.4 mg/L) and ESR (116 mm/Hg). Procalcitonin and tumor biomarkers were normal, and T-SPOT.TB was negative. Enhanced upper abdominal magnetic resonance imaging (MRI) showed right adrenal gland mass (7.6×6.5 cm) hypointensity in the T1-weighted

images and hyperintensity in the T2-weighted images; the mass had a thick wall with an inhomogeneous signal inside (Figure 1C,D,E).

CT-guided percutaneous puncture catheter drainage was performed on the second day, and approximately 300 mL of foul-smelling thick pus was drained for routine examination, smear, culture (including aerobic, anaerobic and fungal cultures) and mNGS detection. The rhythm of the adrenocorticotrophic hormone and cortisol secretion, the renin-angiotensin-aldosterone system (RAAS) hormone level and the secretion of methoxy epinephrine and methoxy norepinephrine were all assessed and were within the normal ranges. Exfoliated tumor cells were not found in the pus. The patient was preliminarily diagnosed with adrenal abscess after finding both gram-positive cocci and gram-negative bacilli in the pus. Therefore, we immediately initiated ertapenem therapy at 1 g every 24 hours intravenously. A transient fever (39.0 °C) with chill was observed 3 hours after drainage, and then, peripheral blood was drawn for culture and mNGS detection. The pus

culture revealed only *Escherichia coli* (d2), *Proteus mirabilis* (d2) and *Actinomyces turicensis* (d5). By contrast, pus mNGS identified multiple pathogens (86% anaerobes) with high reads (including *Peptostreptococcus* 27.9%, *Porphyromonas* 19.2%, *Filifactor* 14.1%, *Pyramidobacter* 11.1%, *Prevotella* 9.9%, *Anaeroglobus* 1.1%, *Bacteroides* 1.1%, *Slackia* 0.9%, and *Fusobacterium* 0.7%) and other microorganisms (including *Escherichia* 0.1%, *Proteus* 0.6%, *Mycoplasma* 1.6% and so on) (Figure 2A). The blood culture was negative, whereas peripheral blood NGS detected multiple pathogens, including 74.6% anaerobes (*Porphyromonas* 30.0%, *Pyramidobacter* 21.2%, *Prevotella* 8.5%, *Filifactor* 6.5%, *Anaeroglobus* 5.5%, and *Solobacterium* 3.1%) (Figure 2B).

The patient was clinically relieved of back pain, and the inflammatory biomarkers, including the WBC count, CRP and ESR, were decreased after completing 16 days of combination antimicrobial therapy and drainage. Pus mNGS revealed dramatically decreased reads and anaerobic numbers (Figure 2C). Repeated upper abdominal enhanced MRI showed an obvious reduction in the size of the adrenal mass (Figure 3). The patient was transitioned to oral maintenance therapy consisting of faropenan at 0.2 g every 8 hours for eleven weeks. The follow-up lab examination of inflammatory biomarkers was normal, and the adrenal mass was reduced radiographically.

Discussion

Adrenal gland abscess is extremely rare in adults. Symptoms of acute adrenal abscess are fever, chills, abdominal pain. Some chronic infection only presents with symptoms of chronic adrenocortical hypofunction due to the disturbance of the hypothalamic-pituitary-adrenal axis. When patients present with complaints, such as abdominal or back pain; fever with elevated lab inflammatory markers; and underlying immunosuppression, such as HIV co-infection, immunosuppressant drug usage or recent surgical procedures, abscessation of the adrenal glands should be considered. The adrenal glands are retroperitoneal with a rich blood supply from several intraperitoneal vessels. The right adrenal gland is more susceptible to hemorrhage due to anatomical differences, accounting for approximately 70% of cases. This case also involved the right adrenal gland, but the patient was not obviously immunocompromised, as mentioned before.

The literature shows that pathogens in adrenal abscesses are diverse (2-4,6-10). *Staphylococcus aureus* and *Escherichia coli* are the most common bacteria in acute infection, while *Tuberculosis*, *Nocardia*, fungi and parasites are more common in chronic infection. We were amazed to find a polymicrobial infection with a large number of anaerobic bacteria in our case. The pathogenesis of this case was ambiguous. The microorganisms detected in our case were mostly from the human oral cavity, some of which have been reported to cause gingivitis, periodontopathy, and among other diseases (11-14). Our patient had previously smoked for more than ten years and had poor oral hygiene, so we hypothesize that the pathogenic microorganisms might have originated from ectopic oral flora and disseminated to the right adrenal gland through the blood, although the patient underwent no dental procedures.

Anaerobic bacteria are common causes of infections, often involving polymicrobial flora, some of which can be serious and life-threatening. Because of their fastidious nature, anaerobes are rarely cultured and isolated, as they require specific inoculation methods and culture equipment. The results of anaerobic cultures are usually received after treatment decisions are made.

mNGS technology takes approximately 2 days to identify microorganisms, whereas culture-based methods take almost 2-7 days. Moreover, mNGS can detect unculturable or difficult-to-culture microorganisms. Unlike specific PCR, mNGS can identify multiple pathogens simultaneously with no prior assumptions (9). Rare cases have reported adrenal gland abscess caused by anaerobes, but no case of multiple anaerobes has been reported, suggesting that their limitations in traditional cultivation methods and that vigilance against anaerobe-induced infections is required.

This case suggests that mNGS technology has the significant advantages of obtaining rapid and accurate etiological diagnoses in suspected anaerobic infection, especially during co-infection with multiple microorganisms. mNGS can provide an important basis for choosing medication in clinical practice.

In conclusion, to our knowledge, this is the first report of an adrenal gland abscess primarily due to multiple anaerobes detected by mNGS analysis. mNGS technology provides rapid and accurate determination of pathogens and has promising value for detecting anaerobes and coinfection with multiple microorganisms in the future.

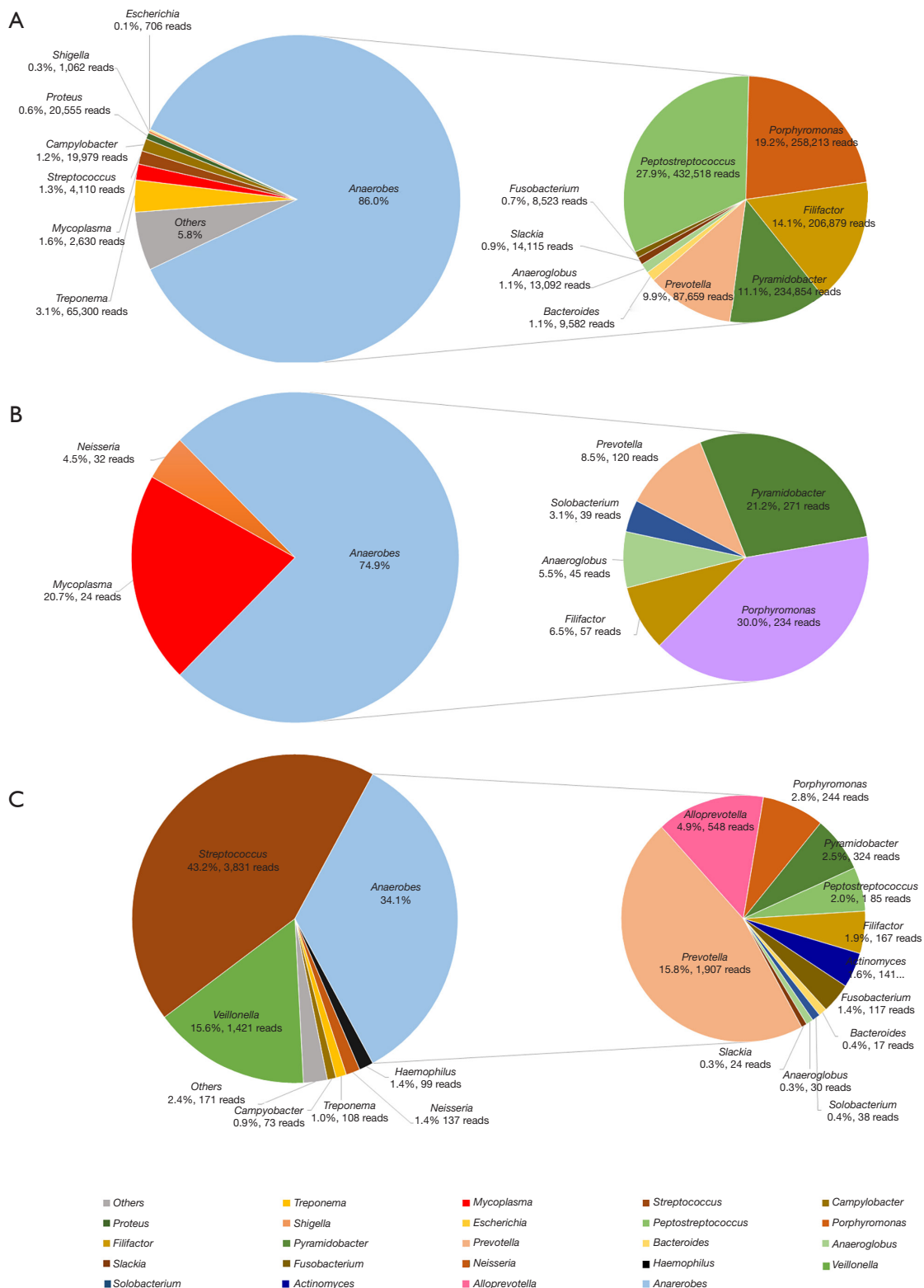


Figure 2 Metagenomic next-generation sequencing results: classification of the sequencing relative abundance at the genus level of different samples were shown. Anaerobes were further classified at genus level. (A) Purulent fluid on the day of catheterization. (B) Peripheral blood on the day of catheterization. (C) Purulent fluid after six days of therapy.

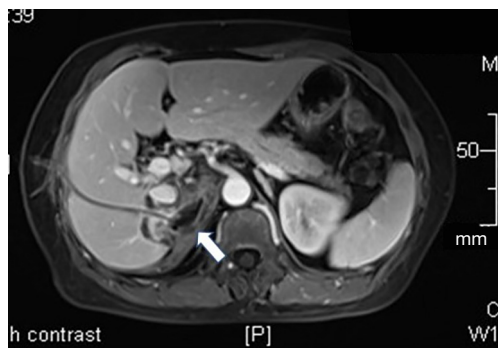


Figure 3 T1-weighted image with contrast after eleven weeks of antimicrobial therapy and drainage.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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