CASE REPORT



Case report: Cervical suppurative lymphadenitis caused by burkholderia multivorans in a healthy child



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Abstract

Background Cervical suppurative lymphadenitis in children is commonly caused by Staphylococcus aureus or Streptococcus pyogenes. However, cases caused by Burkholderia multivorans (BM) are rare. The clinical presentation lacks specificity, making it difficult for clinicians to recognize, which may delay diagnosis and treatment.

Case presentation We report a case of a 5-year-old boy admitted with recurrent fever and neck swelling. Initial treatment with meropenem and linezolid was ineffective, and symptoms persisted after 24 days of conservative therapy. Aspiration of pus yielded negative culture results. Definitive diagnosis was achieved through surgical biopsy of cervical lymph nodes, pathological examination, and metagenomic next-generation sequencing (mNGS), which identified BM as the causative pathogen. The patient was successfully treated with a combination of trimethoprim-sulfamethoxazole and meropenem. The cervical lesion exhibited granulomatous inflammation and was managed with adjunctive vacuum-assisted closure (VAC) therapy, resulting in complete wound healing without recurrence.

Conclusions This study aims to raise awareness among all specialists about BM as a potential causative agent in cervical suppurative lymphadenitis. Early recognition and timely intervention can reduce misdiagnosis and missed diagnoses, improving patient outcomes.

Keywords Cervical suppurative lymphadenitis, Burkholderia multivorans, Healthy child, Precise diagnosis, Granulomatous inflammation

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Background

Cervical suppurative lymphadenitis is a common pediatric infectious disease, typically caused by well-known pyogenic pathogens such as Staphylococcus aureus and Streptococcus pyogenes [1]. Cases attributed to rare or opportunistic pathogens are relatively uncommon. Burkholderia multivorans (BM), an opportunistic pathogen, primarily causes infections under specific conditions or in immunocompromised patients.

It is most commonly associated with chronic pulmonary infections, such as those related to cystic fibrosis, or chronic granulomatous disease [2]. In healthy individuals, BM has been associated with other types of

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infections, including bacterial meningitis [3], sepsis in liver transplant recipients [4], urinary tract infections in otherwise healthy men [5], and certain iatrogenic infections (e.g., peritonitis following abdominal puncture and neonatal postoperative sepsis due to ultrasound gel) [6, 7]. However, cases of isolated cervical lymphadenopathy or suppuration caused by BM have not been reported. As a causative agent of cervical suppurative lymphadenitis in healthy children, BM is exceedingly rare, posing challenges in timely diagnosis and effective treatment.

This case aims to enhance awareness for all specialists (ENT, OMF, pediatrics, etc.) of the potential for rare pathogens in cervical suppurative lymphadenitis. By sharing this experience, we hope to provide valuable insights for the diagnosis and management of similar cases, underscore the importance of considering uncommon pathogens in clinical practice, and ultimately reduce misdiagnoses and missed diagnoses while improving patient care outcomes.

Case presentation

A 5-year-old boy was admitted with a one-week history of recurrent fever and neck swelling. The symptoms began suddenly with episodes of high fever, peaking above 39.0 °C, occurring 3-4 times daily. Bilateral neck swelling and tenderness were also noted. No symptoms such as vomiting, diarrhea, cough, wheezing, rash, red

eyes, lip chapping, sclerema, gum bleeding, limb pain, movement disorders, or other clinical manifestations were observed. Ultrasound revealed bilateral cervical lymphadenopathy, with multiple hypoechoic nodules detected on both sides. The largest nodule on the right side measured approximately 2.6×1.0 cm, while the largest on the left measured approximately 1.9×1.0 cm. All nodules had well-defined margins and homogeneous internal echogenicity, with no anechoic areas detected. The patient received intravenous penicillin and metronidazole for a total of six days at the referring hospital. The exact dosages were not recorded in the medical history upon admission. His neck pain worsened, prompting referral to our institution. He was admitted with a diagnosis of "bilateral cervical lymphadenitis." The patient had a previously healthy medical history with no known hereditary conditions, infectious diseases, or long-term medication use(Fig. 1).

On admission, physical examination revealed bilateral cervical swelling with significant tenderness. Multiple enlarged lymph nodes were palpable, the largest on the right side measuring approximately 2.5×1.0 cm. The overlying skin was smooth, and the nodes were mobile. No other positive signs. The laboratory and imaging findings were as follows: Complete blood count (CBC): White



Fig. 1 This is an image of a swollen neck. The black arrow indicates the area with the most significant swelling. The labels 'R' and 'L' mark the right and left sides, respectively

blood cell (WBC) count was 17.41×10^9 /L, with a neutrophil percentage of 78.7% and a lymphocyte percentage of 15.2%. Inflammatory markers: C-reactive protein (CRP): 25 mg/L, Serum amyloid A (SAA): >320 mg/L, Erythrocyte sedimentation rate (ESR): 29 mm/h, Interleukin-6 (IL-6): 137 pg/mL, Interleukin-2, -4, and -10 were within normal ranges. Immunoglobulin levels (IgG, IgA, IgM): Within normal limits. Epstein-Barr virus (EBV) capsid antigen (VCA) IgG and EBV nuclear antigen (EBNA) IgG were positive. EBV VCA IgM, EBNA IgM, EBV early antigen (EA) IgG, and EBV DNA quantification were negative. Cytomegalovirus (CMV) IgM and CMV DNA quantification were negative. Respiratory pathogen screening: Negative for respiratory syncytial virus, adenovirus, influenza virus, parainfluenza virus, Mycoplasma pneumoniae, Chlamydia pneumoniae, and Legionella spp.

Other tests: Procalcitonin (PCT), rheumatoid factor (RF), immunoglobulin levels, complement levels, anti-streptolysin O (ASO) titer, and ferritin were within normal ranges. Blood cultures were negative. Tumor necrosis factor-alpha (TNF- α) and interferon-gamma (IFN- γ) levels were normal. Lymphocyte subset absolute counts were within normal limits. Antinuclear antibody (ANA) test and purified protein derivative (PPD) test were negative.

Imaging Findings: Color ultrasound of heart and abdominal cavity (including liver, gallbladder, spleen and pancreas) showed no obvious abnormality.

Based on these findings, the differential diagnosis included bacterial (e.g., Staphylococcus aureus, Streptococcus spp., Mycobacterium tuberculosis, nontuberculous mycobacteria), viral (EBV, CMV), and autoimmune causes (e.g., Kawasaki disease, sarcoidosis). The normal immunoglobulin levels and negative ANA/PPD tests reduced the likelihood of autoimmune or tuberculosisrelated etiologies. Given the predominance of neutrophilia and elevated inflammatory markers, a bacterial etiology was strongly suspected. Cefotaxime was selected as an empirical antibiotic. Initial treatment with cefotaxime, administered at a dose of 50 mg/kg every 12 h, did not resolve the symptoms. The child continued to have recurrent fever, with a maximum temperature reaching 39 °C, and cervical swelling increased compared to before. After two days of administration, the antibiotic was escalated to meropenem, which has a broader spectrum and is more effective against resistant bacteria, at a dosage of 20 mg/kg every 8 h. Following the initiation of meropenem, the child's fever peaks gradually decreased, with body temperature ranging between 37.5 and 38 °C. However, cervical swelling and pain showed no improvement.

After 10 days of meropenem treatment, the child's fever recurred, with a maximum temperature of 38.5 °C,

and cervical swelling and pain persisted. A repeat blood test revealed elevated inflammatory markers (WBC: 11.84×10⁹/L, NEUT%: 76%, CRP: 27.03 mg/L). Considering the lack of significant response and the possibility of Gram-positive pathogens, linezolid was added intravenously to broaden the coverage, particularly against multidrug-resistant Gram-positive bacteria, including MRSA and other resistant species. Ultrasound re-evaluation revealed bilateral suppurative cervical lymphadenitis. The largest lymph nodes measured 2.5×1.5 cm on the left and 3.9×1.4 cm on the right, with small anechoic areas observed within the nodes. Under ultrasound guidance, aspiration was performed on the purulent lymph node, yielding 0.2mL of white pus. The pus was subjected to culture (including standard bacterial culture and Haemophilus-specific culture) and smear microscopy with acid-fast staining, all of which returned negative results. Additionally, repeated blood culture results were also negative.

Despite 12 days of combined meropenem and linezolid therapy, the patient experienced recurrent highgrade fevers (up to 39 °C), persistent lymphadenopathy, and worsening inflammatory markers (CRP: 46 mg/L). Contrast-enhanced MRI of the neck revealed multiple enlarged lymph nodes with partial fusion, heterogeneous signals, and high diffusion-weighted imaging (DWI) signals in the cervical and supraclavicular regions. Adjacent soft tissues, including the parotid and submandibular glands, were involved, suggesting necrotic lymphadenitis with surrounding soft tissue infection (Fig. 2).

Under general anesthesia, bilateral cervical lymph node biopsy was performed. Ultrasound guidance was used preoperatively to aid in identifying the most affected lymph nodes for surgical excision. Intraoperatively, multiple fused lymph nodes were identified. The largest necrotic nodes were excised, yielding approximately 1 mL of yellow-white purulent fluid. Pathological examination revealed suppurative granulomatous lymphadenitis. Metagenomic next-generation sequencing (mNGS) of the pus identified BM as the causative pathogen. The identified pathogen was detected through high-throughput sequencing of purulent fluid obtained via ultrasoundguided aspiration from the affected lymph node, which supports its potential pathogenic role rather than being a commensal. Given the absence of recurrent respiratory symptoms, pancreatic insufficiency, or other clinical indicators, cystic fibrosis genetic testing was not performed, as there was no strong suspicion of an underlying CFrelated immunodeficiency.

Based on published articles and Sanford guide, we adjusted the antibiotic regimen to intravenous meropenem combined with oral trimethoprim-sulfamethoxa-zole (SMZ-TMP). The dosage of SMZ-TMP (SMZ 0.4 g, TMP 80 mg) was taken orally twice daily. Meropenem



Fig. 2 Cervical contrast-enhanced MRI: T1-weighted imaging with contrast enhancement (T1W+C) shows uneven and marked enhancement with high signal intensity, accompanied by cystic non-enhancing areas (black arrow)

was administered at 20 mg/kg every 8 h via intravenous injection. The patient's fever subsided, and his condition improved significantly. Cervical pain and swelling gradually resolved. Additional screening for other infection foci, including chest X-rays, abdominal ultrasound, and urine cultures, showed no abnormalities. After 14 days of combined therapy, the patient's inflammatory markers normalized, and he was discharged in stable condition.

After discharge, the surgical incisions on both sides of the patient's neck exhibited delayed healing, with visible granulation tissue and purulent discharge. Despite regular wound care for one month, there was no significant improvement in wound healing. For further wound management, the patient was readmitted. Under general anesthesia, thorough debridement of both cervical wounds was performed, with the removal of necrotic tissue and purulent exudates. Vacuum-assisted closure (VAC) therapy was applied with a negative pressure of -75 mmHg. After seven days, the VAC device was removed, revealing fresh granulation tissue with no necrotic tissue or purulent discharge. Subsequently, surgical wound closure was performed.

The patient recovered well and was discharged without complications. During a six-month follow-up, no recurrence of infection was observed, and the surgical wound had healed completely.

Discussion

Cervical suppurative lymphadenitis is characterized by acute inflammation and pus formation, typically presenting with localized neck swelling, tenderness, and fever. Common pathogens include Staphylococcus aureus and Streptococcus species [8], while infections caused by BM are rare. This case provides a new diagnostic and therapeutic approach for complex cervical suppurative lymphadenitis unresponsive to prolonged antibiotic treatment, revealing the potential complexity of its etiology. It also highlights the importance of recognizing rare infections, reducing misdiagnoses, and improving clinical treatment.

The clinical presentation of this child with recurrent fever, bilateral neck swelling, and tenderness over the course of one week poses a diagnostic challenge, requiring a thorough differential diagnosis. The initial clinical suspicion was pyogenic lymphadenitis, likely of bacterial origin, and empirical treatment with intravenous cefotaxime was initiated. However, the lack of clinical improvement raised concern for resistant or atypical pathogens, necessitating further investigation and more targeted therapy.

The differential diagnosis for bacterial pyogenic lymphadenitis includes common pathogens such as Staphylococcus aureus and Streptococcus pyogenes, which are frequently implicated in pediatric cervical lymphadenitis. These pathogens typically present with acute onset of localized pain, redness, and swelling, which often progress rapidly. In this case, however, despite appropriate initial antibiotic therapy, the lack of significant clinical improvement raises the possibility of infection with more resistant organisms, such as MRSA or less common pathogens [8].

Additionally, granulomatous lymphadenitis in the head and neck region, often caused by Bartonella or nontuberculous mycobacteria (NTM), should also be considered. Bartonella, the causative agent of cat scratch disease, is known to cause localized lymphadenopathy, often with a chronic course. However, the patient had no history of cat or animal contact, normal liver function, and no enlargement of the liver or spleen on ultrasound, which makes this diagnosis less likely. The patient's negative tuberculin skin test and absence of granulomatous changes on imaging make tuberculosis and sarcoidosis less likely [9].

While bacterial pathogens remain the most common cause of pyogenic lymphadenitis, viral infections, particularly EBV and CMV, must also be considered in the differential. EBV is a well-established cause of infectious mononucleosis, often presenting with fever, lymphadenopathy, and fatigue. The patient's EBV serology indicated past exposure (positive VCA IgG and EBNA IgG), but the absence of acute EBV markers (e.g., VCA IgM, EA IgG, and EBV DNA) made active EBV infection unlikely. CMV was also ruled out, as both IgM and CMV DNA quantification were negative. Given the negative viral screening results and the clinical course, a viral etiology is less likely in this case.

Autoimmune conditions, such as Kawasaki disease and sarcoidosis, can present with systemic inflammation and lymphadenopathy. However, Kawasaki disease typically presents with mucocutaneous signs such as conjunctival injection, lip chapping, and rash, none of which were observed in this patient [10]. Furthermore, sarcoidosis is more commonly diagnosed in older children or adults, and is usually associated with bilateral hilar lymphadenopathy, pulmonary involvement, and granulomatous inflammation, which were not seen in this case. The negative results for ANA and PPD testing further excluded autoimmune and infectious etiologies like tuberculosis or sarcoidosis.

In the absence of clinical response to initial empirical therapy, the infection was initially suspected to be caused by a drug-resistant bacterial pathogen. The patient was subsequently treated with a restricted antibiotic regimen, but the condition continued to worsen. Given the lack of response to standard treatment, BM infection was ultimately diagnosed through surgical biopsy specimens and pus samples using mNGS, which provided definitive evidence of an atypical pathogen. This result guided the selection of appropriate targeted antibiotics.

BM belongs to the Burkholderia genus, which is part of the Burkholderia cepacia complex (Bcc). The Burkholderia cepacia complex is an opportunistic pathogen that generally poses minimal risk to healthy individuals. The clinical manifestations of Bcc infections range from asymptomatic chronic infections to acute, life-threatening conditions such as necrotizing pneumonia, acute respiratory distress syndrome, and bacteremia (referred to as "onion syndrome"), with a mortality rate as high as 75% [11]. BM is a species within the Bcc that rarely causes "onion syndrome," even in patients with cystic fibrosis. A study has shown that infections caused by Burkholderia cenocepacia or Burkholderia orbicola result in a higher risk of post-transplant sepsis compared to infections caused by BM [12].

In recent years, there have been reports of bacteremia caused by BM in children and neonates, most commonly in those with immunodeficiency (such as chronic granulomatous disease), other underlying conditions or noso-comial infection [4, 13, 14]. However, there have been

no reports of cervical lymphadenopathy or suppuration as clinical manifestations of BM infections. The case we present involves a previously healthy child who developed fever, cervical lymphadenopathy, and suppuration, with no underlying immunodeficiency, pulmonary disease, or other predisposing conditions. This case is rare in clinical practice, making it easy to overlook, which may lead to delayed diagnosis and treatment.

Burkholderia species possess intrinsic resistance to multiple classes of antibiotics, which may explain the failure of the initial antibiotic therapy in this case. Following the mNGS results, a combined treatment regimen of meropenem and trimethoprim-sulfamethoxazole proved effective, leading to resolution of the fever and improvement in lymphadenitis.

Burkholderia species, including BM, exhibit resistance to polymyxin B and many first-line antibiotics due to their unique membrane structure. Efflux pumps actively expel antibiotics such as β -lactams and fluoroquinolones, reducing their effectiveness. Many strains produce β -lactamases, including extended-spectrum β -lactamases (ESBLs), which degrade β -lactam antibiotics and confer resistance to third- and fourth-generation cephalosporins. The outer membrane of Burkholderia species, rich in lipopolysaccharides and phospholipids, makes it impermeable to many antibiotics, such as aminoglycosides [15]. Therefore, Burkholderia species are notably resistant to several antibiotics, including β -lactams (e.g., penicillin, cephalosporins) and exhibit varying levels of resistance to aminoglycosides and quinolones. However, they are typically susceptible to trimethoprim-sulfamethoxazole (SMZ-TMP), which is the first-line treatment for Burkholderia infections. When patients are allergic or intolerant to SMZ-TMP, or when the pathogen is resistant to it, the most effective alternative options include levofloxacin, meropenem, minocycline, and ceftazidime [2]. In this case, the patient responded well to combined treatment with SMZ-TMP and meropenem, highlighting the importance of precise antimicrobial selection in treating BM infections.

The delayed wound healing and granulation tissue formation after lymph node biopsy suggest that BM infection may exacerbate localized granulomatous inflammation, complicating wound closure. Aggressive debridement and VAC therapy were successfully employed to control the infection and promote wound healing, demonstrating the value of a comprehensive treatment strategy in managing complex infections.

The diagnosis of BM in this case was particularly challenging. Culturing BM requires specific conditions, including the selection of appropriate growth media, optimal incubation temperature (35–37 °C), and an aerobic environment. While BM can grow on standard media such as nutrient agar and blood agar, selective media, such as Burkholderia cepacia selective agar (BCSA), are often preferred due to their ability to suppress other microorganisms and promote the growth of Bcc species. Other selective media, including Oxidation-Fermentation Polymyxin B Lactose Agar (OFPBL) and Pseudomonas cepacia agar (PCA), are also used. However, BM grows slowly, even on selective media, and typically requires 48–72 h for visible colony formation, which complicates diagnosis further. Challenges arise from the slow-growing nature of BM, and the influence of factors such as bacterial load and prior antibiotic exposure, which may inhibit growth and lead to false-negative results, as seen in our case [16].

Modern molecular techniques are essential for overcoming these challenges and ensuring accurate species identification. Due to the close genetic relationship between members of the Bcc, biochemical tests alone often fail to provide accurate identification, leading to misdiagnosis. Biochemical tests, such as oxidationfermentation and polymyxin B resistance, provide preliminary identification, but Matrix-Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS), Polymerase Chain Reaction (PCR), and 16 S rRNA sequencing offer faster and more precise methods for confirming BM. The genetic variation among Bcc species is minimal, and while MALDI-TOF MS can rapidly identify the genus, its species-level accuracy may be limited. PCR targeting specific genes, such as recA, offers high sensitivity for species confirmation. Additionally, 16 S rRNA sequencing can also be used, but with lower species resolution [17]. mNGS provides the advantage of detecting bacterial DNA, including from non-viable or dormant bacteria, making it especially useful when traditional culture methods are hindered, as in our case where prior antibiotic use likely reduced the bacterial load. These molecular techniques play a critical role in the rapid and accurate diagnosis of BM, particularly when conventional methods may not yield reliable results.

Conclusion

Cervical suppurative lymphadenitis caused by BM is rare in healthy children, presenting with subtle and nonspecific symptoms, which can lead to misdiagnosis and inappropriate treatment. In cases of complex suppurative lymphadenitis with poor response to antibiotic therapy, it is important to consider rare pathogens in addition to tuberculosis, multidrug-resistant organisms, and tumors. Early use of advanced microbiological diagnostic techniques, including mNGS, helps confirm the diagnosis promptly and guide clinical treatment. Furthermore, for patients with localized infections complicated by granulomatous inflammation, active debridement and infection control are crucial.

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Author contributions

B.B.N. and J.J.X. drafted the manuscript, collected the data and reviewed the literature. J.A.L. and L.D.Z. substantively revised the manuscript. All authors read and approved the final manuscript.

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Data availability

All data and materials are presented in the manuscript.

Declarations

Ethics approval and consent to participate

Ethics approval was obtained from the Ethics Committees of the Children's Hospital Affiliated to Shandong University (Jinan Children's Hospital).

Consent for publication

Written informed consent for the publication of this case report was obtained from both the patient and their guardian.

Competing interests

The authors declare no competing interests.

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