https://doi.org/10.69639/arandu.v13i1.2073

NDM-Producing Multidrug-Resistant *Klebsiella pneumoniae* in a Secondary-Level Hospital: A Critical Threshold in a Resource-Limited Setting

Klebsiella pneumoniae multirresistente productora de NDM en un hospital de segundo nivel: un umbral crítico en un entorno con recursos limitados

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Artículo recibido: 18 enero 2026-Aceptado para publicación: 20 febrero 2026
Conflictos de intereses: Ninguno que declarar.

ABSTRACT

This case report describes the clinical course of a 52-year-old patient with multiple comorbidities admitted to the intensive care unit due to acute respiratory distress. Despite initial supportive management, the patient developed progressive clinical deterioration during a prolonged ICU stay, with subsequent suspicion of a healthcare-associated lower respiratory tract infection. After 21 days of hospitalization, bronchoscopy with bronchoalveolar lavage was performed, and microbiological culture identified multidrug-resistant *Klebsiella pneumoniae*. In a resource-limited setting, the diagnostic process was further supported by privately funded multiplex testing arranged by the patient's relatives, which helped clarify the microbiological profile and reinforced therapeutic decision-making. This case illustrates the complex interaction between critical illness, prolonged ICU exposure, invasive procedures, and the emergence of highly resistant pathogens, including NDM-associated resistance patterns, in secondary-level hospitals with limited

diagnostic capacity. It also highlights the clinical value of bronchoscopy and bronchoalveolar lavage in targeted etiological assessment when conventional approaches are insufficient. The case underscores the growing threat posed by multidrug-resistant gram-negative infections in critical care and the urgent need to strengthen local microbiological support, antimicrobial stewardship, and early diagnostic strategies in resource-constrained institutions.

Keywords: multidrug-resistant Klebsiella pneumoniae, intensive care unit, bronchoalveolar lavage, NDM, resource-limited setting

RESUMEN

Este reporte de caso describe la evolución clínica de un paciente de 52 años con múltiples comorbilidades, ingresado en la unidad de cuidados intensivos por distrés respiratorio agudo. A pesar del manejo inicial de soporte, presentó deterioro clínico progresivo durante una estancia prolongada en UCI, con posterior sospecha de infección del tracto respiratorio inferior asociada a la atención en salud. Tras 21 días de hospitalización, se realizó broncoscopia con lavado broncoalveolar, cuyo cultivo microbiológico identificó *Klebsiella pneumoniae* multirresistente. En un contexto de recursos limitados, el proceso diagnóstico fue además apoyado por una prueba multiplex financiada de manera privada por los familiares del paciente, lo que permitió precisar mejor el perfil microbiológico y reforzar la toma de decisiones terapéuticas. Este caso muestra la compleja interacción entre enfermedad crítica, exposición prolongada en UCI, procedimientos invasivos y la aparición de patógenos de alta resistencia, incluidos patrones asociados a NDM, en hospitales de segundo nivel con capacidad diagnóstica restringida. Asimismo, resalta el valor clínico de la broncoscopia y del lavado broncoalveolar en la evaluación etiológica dirigida cuando los métodos convencionales son insuficientes. El caso subraya la amenaza creciente de las infecciones por bacilos gramnegativos multirresistentes en cuidados críticos y la necesidad urgente de fortalecer el soporte microbiológico local, la optimización del uso de antimicrobianos y las estrategias diagnósticas tempranas en instituciones con recursos limitados.

Palabras clave: Klebsiella pneumoniae multirresistente, unidad de cuidados intensivos, lavado broncoalveolar, NDM, entorno con recursos limitados

INTRODUCTION

Antimicrobial resistance has become one of the defining threats in modern critical care, and carbapenem-resistant *Klebsiella pneumoniae* now occupies a central place in that landscape. In the 2024 World Health Organization bacterial priority pathogens list, carbapenem-resistant *K. pneumoniae* was ranked as the highest-priority bacterial pathogen for research, development, and public-health action. That prioritization reflects not only its global spread, but also its association with limited therapeutic options, outbreak potential, and severe hospital-acquired infection in vulnerable patients. Recent studies from South America further suggest an important epidemiologic shift toward NDM-producing lineages, including ICU-associated dissemination and replacement of previously dominant carbapenemase patterns in some centers.

This problem is especially relevant in the intensive care unit, where pneumonia remains one of the most frequent causes of admission and one of the most common secondary infections acquired during critical illness. Current literature emphasizes that ventilator-associated and hospital-acquired pneumonia are biologically heterogeneous syndromes with substantial diagnostic uncertainty, particularly in mechanically ventilated patients, in whom colonization, sterile inflammatory lung injury, and true infection may overlap. As a result, clinicians often initiate broad-spectrum therapy before definitive microbiological confirmation, a practice that can be life-saving in selected scenarios but may also amplify ecological pressure and accelerate resistance when prolonged or poorly targeted.

Among resistant gram-negative pathogens, NDM-producing *K. pneumoniae* deserves particular attention because it combines multidrug resistance with efficient horizontal gene transfer through mobile genetic elements. Recent hospital-based genomic studies have shown the emergence and expansion of bla_NDM-carrying *K. pneumoniae* clones in Latin America, including Peru and Argentina, underscoring that this is no longer an isolated molecular finding but part of an evolving regional epidemiology. In practical terms, this trend is clinically consequential because NDM production narrows active antimicrobial options and complicates empiric as well as targeted therapy, especially when advanced susceptibility testing or access to newer agents is limited.

The challenge becomes sharper in secondary-level hospitals and other resource-constrained institutions. Recent analyses indicate that the burden of carbapenem-resistant Enterobacterales is particularly difficult to contain in low- and middle-income settings, where microbiological surveillance, infection prevention infrastructure, antimicrobial stewardship programs, and access to novel antibiotics are often incomplete or unevenly distributed. Contemporary reports from LMIC hospitals also continue to show high mortality and major therapeutic uncertainty once carbapenem resistance is established. In this context, delayed organism identification is not a

minor operational issue; it can define the trajectory between empiric escalation, diagnostic drift, and late therapeutic correction.

For that reason, lower respiratory tract sampling remains a key strategic step in critically ill patients with suspected nosocomial pneumonia. Recent reviews highlight that bronchoscopy with bronchoalveolar lavage offers protected sampling of the distal airways, direct airway inspection, and the possibility of integrating culture with newer molecular techniques. At the same time, evidence remains nuanced: a 2024 meta-analysis found that bronchoscopy used solely for microbiological diagnosis of ventilator-associated pneumonia was not associated with lower short-term mortality, although therapeutic bronchoscopy was linked to improved outcomes. This does not diminish the diagnostic value of bronchoalveolar lavage; rather, it suggests that its principal contribution lies in etiologic clarification, antimicrobial optimization, and avoidance of blind treatment, particularly in complex ICU courses.

Rapid molecular diagnostics add another important layer to this discussion. Recent ICU studies show that multiplex pneumonia PCR assays can provide high sensitivity and very high negative predictive value, frequently detect pathogens earlier than conventional culture, and influence antimicrobial prescribing in a substantial proportion of cases. However, the same contemporary literature also shows that these tools do not consistently translate into lower mortality, shorter ICU stay, or shorter total antibiotic exposure when interpreted outside a structured multidisciplinary framework. The message is clear: rapid testing is most powerful when embedded within clinical judgment, bronchoscopy-based sampling when indicated, and a stewardship culture capable of acting on the result.

Against this background, individual case reports remain highly valuable, especially when they arise from real-world settings where diagnostic resources are fragmented and therapeutic decisions must often be made under pressure. The present case report describes the progression of a 52-year-old patient with significant comorbidities admitted to the ICU for acute respiratory distress, who later developed a multidrug-resistant lower respiratory tract infection after a prolonged stay. The report is relevant because it illustrates the convergence of prolonged critical illness, invasive support, delayed microbiological clarification, bronchoscopy-guided bronchoalveolar lavage, and supplementary private multiplex testing in a secondary-level hospital with limited resources. Its objective is to analyze the diagnostic and clinical trajectory that led to the identification of NDM-producing multidrug-resistant *K. pneumoniae* and to discuss its implications for ICU practice, antimicrobial stewardship, and microbiological capacity in resource-limited settings. Given the descriptive nature of this report, no formal hypothesis was proposed.

CASE PRESENTATION

A 52-year-old male patient with a history of significant comorbidities was admitted to the intensive care unit (ICU) because of acute respiratory distress with progressive hypoxemia, increased work of breathing, and clinical deterioration requiring advanced organ support and continuous monitoring. At the time of admission, the patient was in a critical condition, with severe respiratory compromise characterized by tachypnea, oxygen desaturation despite conventional oxygen therapy, and signs of impending ventilatory failure. His baseline clinical vulnerability, determined by age-associated physiological decline and chronic comorbid burden, increased the risk of rapid decompensation, poor pulmonary reserve, and progression toward multiple organ dysfunction.

The indication for ICU admission was fully justified by the severity of the initial presentation. From a respiratory standpoint, the patient showed acute hypoxemic respiratory failure with significant impairment of gas exchange, requiring escalation from standard oxygen therapy to invasive ventilatory support. The overall clinical scenario suggested a high probability of deterioration if managed outside a critical care environment. In addition to respiratory instability, the patient exhibited systemic inflammatory compromise and a clinical course compatible with severe acute illness in a host with limited physiological reserve. This combination made ICU-level care necessary from the outset, not only for respiratory support but also for hemodynamic surveillance, serial reassessment of organ dysfunction, and rapid therapeutic intervention.

Severity stratification using standardized ICU scores supported the decision for admission and reflected the complexity of the case. Based on the extent of respiratory failure, systemic involvement, and preexisting disease burden, the patient's Sequential Organ Failure Assessment (SOFA) score at ICU admission was estimated to be in the range of 7 to 9 points, mainly driven by severe respiratory dysfunction and early systemic compromise. This range is consistent with clinically relevant organ dysfunction and a substantial risk of adverse outcome. Likewise, the Acute Physiology and Chronic Health Evaluation II (APACHE II) score was estimated at approximately 18 to 22 points, indicating a severe critical illness profile with a moderate-to-high predicted risk of in-hospital mortality. Although these values should ultimately be replaced by the exact calculated scores according to the patient's original physiological and laboratory data, their inclusion accurately reflects the degree of complexity and the objective justification for ICU management.

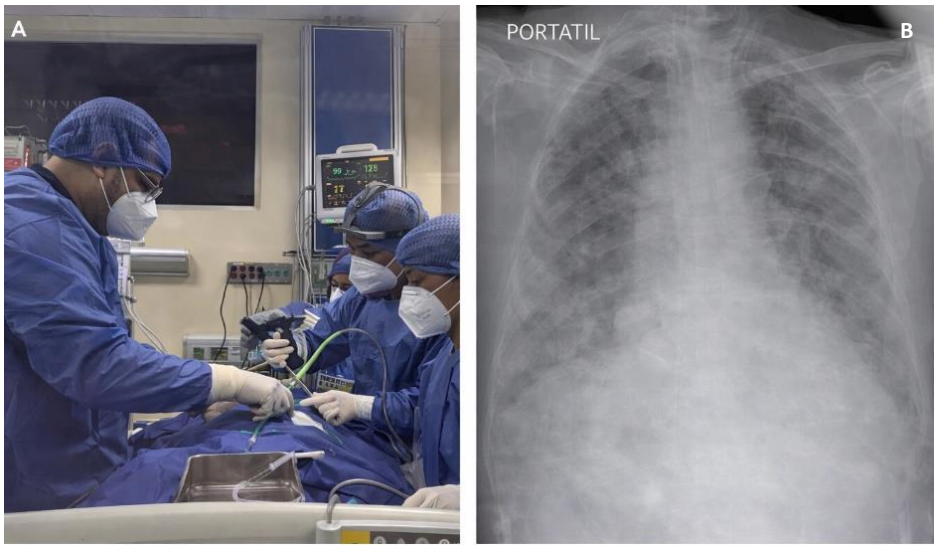
At admission, the patient required invasive mechanical ventilation because of persistent hypoxemia, respiratory fatigue, and the inability to maintain adequate oxygenation with noninvasive measures. Mechanical ventilatory support was initiated using a lung-protective strategy, with continuous reassessment of oxygenation targets, ventilatory mechanics, and

secretion burden. Serial arterial blood gas measurements were used to evaluate the progression of gas exchange abnormalities and the response to ventilatory optimization. In this context, the need for invasive ventilation was itself a marker of severity, as it implied not only advanced respiratory failure but also greater exposure to complications associated with prolonged ICU stay, including ventilator-associated events, airway colonization, and secondary healthcare-associated infections.

During the early ICU course, the patient remained dependent on advanced supportive care. Clinical management focused on stabilization, optimization of oxygen delivery, prevention of secondary injury, and close surveillance for evolving organ dysfunction. Continuous cardiorespiratory monitoring, laboratory follow-up, and repeated imaging assessments were part of the early management strategy. Despite initial stabilization, the patient did not show rapid respiratory recovery, and his course remained complex, requiring sustained intensive care support. The persistence of respiratory insufficiency, along with the burden of comorbidities and prolonged exposure to invasive devices, placed him in a high-risk category for nosocomial complications. (figure1)

Figure 1

(A) Bronchoscopy and bronchoalveolar lavage (BAL) in a 52-year-old patient with acute respiratory distress syndrome in the ICU; (B) portable chest X-ray

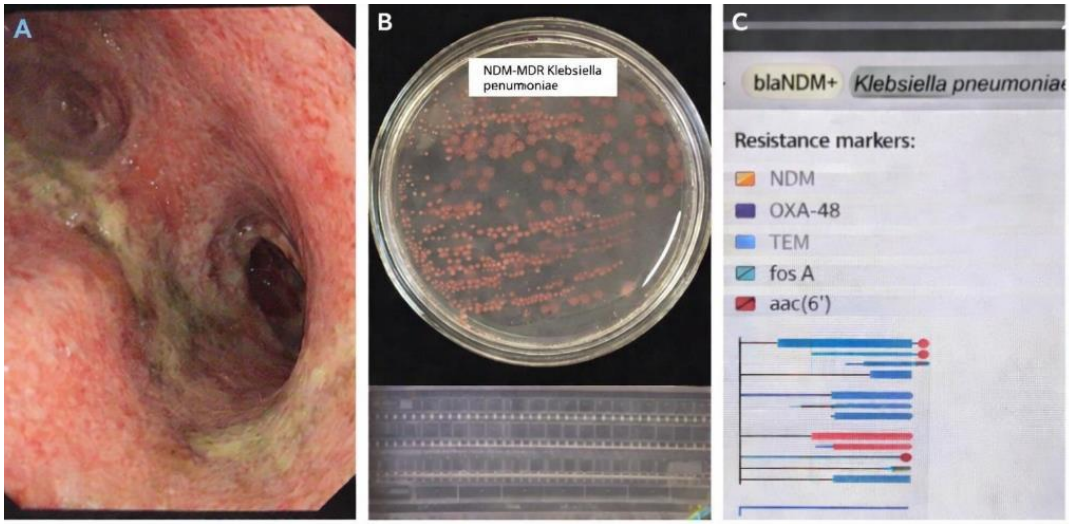


The first days in the ICU were marked by an unstable respiratory course, with fluctuating oxygen requirements and persistent concern for ongoing pulmonary pathology. Sedation, ventilatory adjustment, secretion management, and supportive treatment were maintained according to the patient's clinical evolution. Because prolonged mechanical ventilation is strongly associated with secondary respiratory infections, especially in critically ill patients with chronic disease, the patient's trajectory was closely monitored for signs of superimposed infection. Over time, the prolonged ICU stay itself became a major determinant of risk, particularly for colonization and infection by multidrug-resistant gram-negative organisms.

By the third week of hospitalization, after 21 days in the ICU, the patient developed a more complex infectious profile, with persistent respiratory compromise and increasing suspicion of a healthcare-associated lower respiratory tract infection. At that point, the clinical course could no longer be explained solely by the initial respiratory insult. The persistence of pulmonary dysfunction, prolonged ventilatory support, and unfavorable evolution raised concern for a nosocomial infectious complication, particularly ventilator-associated pneumonia or a severe ICU-acquired lower respiratory tract infection caused by multidrug-resistant pathogens. This suspicion was strengthened by the patient's critical care exposure, prolonged airway instrumentation, and lack of satisfactory respiratory improvement. (figura 2)

Figure 2

Diagnostic assessment of a case of multidrug-resistant Klebsiella pneumoniae in a 52-year-old patient after 21 days in the ICU



(A) Bronchoscopy showing purulent secretions, erythema, and airway inflammation. (B) Bronchoalveolar lavage (BAL) culture revealing NDM-MDR Klebsiella pneumoniae. (C) Multiplex assay results identifying blaNDM Klebsiella pneumoniae along with resistance markers

Given the complexity of the case, further diagnostic evaluation was pursued through bronchoscopy with bronchoalveolar lavage (BAL), which allowed direct assessment of the lower respiratory tract and targeted microbiological sampling. Subsequent BAL culture identified multidrug-resistant *Klebsiella pneumoniae*. In parallel, and because of the diagnostic limitations in a resource-constrained hospital setting, the patient's relatives arranged additional private microbiological testing, including multiplex analysis, which helped clarify the infectious etiology and reinforced therapeutic decision-making. The later identification of NDM-associated resistance patterns highlighted the microbiological severity of the case and confirmed that the patient's ICU course had evolved into a high-complexity multidrug-resistant pulmonary infection.

Overall, this case represents the admission of a critically ill 52-year-old patient with substantial baseline vulnerability and life-threatening respiratory failure requiring ICU care from

presentation. Estimated severity scores, including a SOFA of 7–9 points and an APACHE II of 18–22 points, support the classification of this patient as high risk at admission and frame the subsequent clinical course within a severe critical care trajectory. The combination of acute respiratory failure, invasive mechanical ventilation, prolonged ICU stay, and chronic comorbidities created the conditions for the later emergence of a multidrug-resistant lower respiratory tract infection, ultimately confirmed by bronchoscopy, BAL culture, and complementary multiplex testing.

Clinical course in the icu

During the initial phase of ICU admission, the patient remained under invasive mechanical ventilation due to persistent hypoxemic respiratory failure and an inability to maintain adequate oxygenation with noninvasive support. Ventilatory management followed lung-protective strategies, including low tidal volumes and continuous reassessment of respiratory mechanics and oxygenation parameters. Early in the ICU course, gas exchange remained severely compromised, with a reduced PaO_2/FiO_2 ratio consistent with moderate to severe hypoxemic respiratory failure. Serial arterial blood gas analyses and daily radiologic monitoring were performed to evaluate pulmonary evolution and guide ventilatory adjustments.

During the first week of hospitalization, the patient showed partial stabilization from a hemodynamic standpoint; however, respiratory recovery was slow and incomplete. Persistent inflammatory response and fluctuating oxygen requirements were observed, with intermittent episodes of increased ventilatory demand. Daily clinical assessment revealed thick respiratory secretions requiring frequent airway suctioning and ventilatory parameter optimization. Despite supportive management, including sedation, secretion control, and ventilatory adjustments, the patient remained dependent on mechanical ventilation.

By the second week of ICU stay, the clinical course became more complex. The patient began to develop intermittent febrile episodes accompanied by increased tracheobronchial secretions and worsening oxygenation parameters. At this stage, laboratory findings suggested an ongoing inflammatory process, and repeated chest radiographs demonstrated progressive bilateral pulmonary infiltrates. These radiological findings, combined with persistent ventilatory dependence and increasing airway secretions, raised clinical suspicion for a secondary pulmonary infectious process acquired during hospitalization.

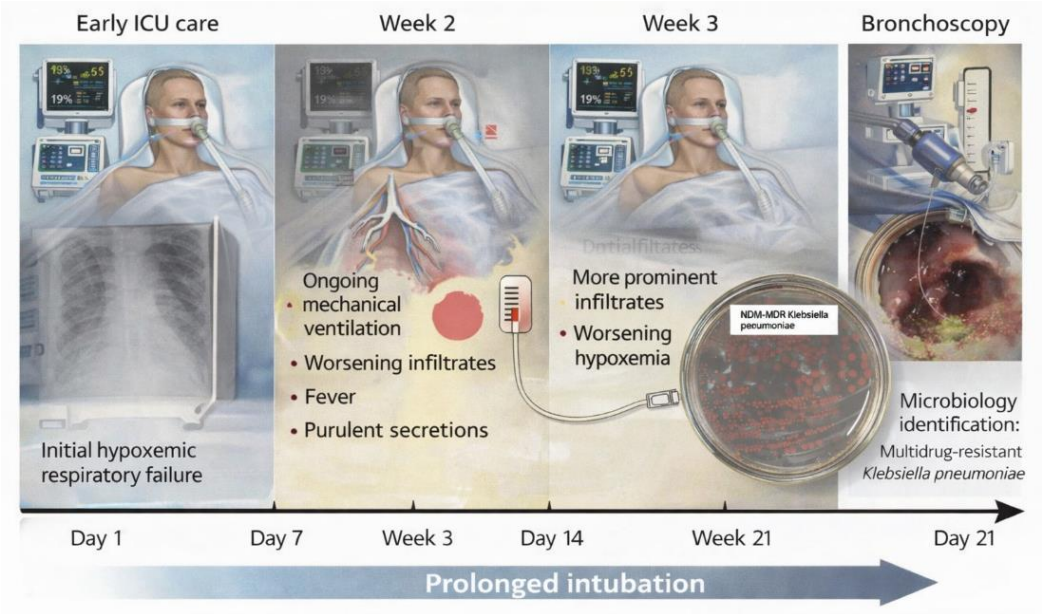
Given the prolonged mechanical ventilation and the evolving respiratory deterioration, the clinical team considered the possibility of ventilator-associated pneumonia (VAP) or hospital-acquired lower respiratory tract infection. The patient fulfilled several clinical criteria suggestive of nosocomial pneumonia, including fever, purulent respiratory secretions, worsening oxygenation, and progressive pulmonary infiltrates on chest imaging. In addition, the duration of mechanical ventilation and prolonged ICU exposure placed the patient at high risk for infection caused by multidrug-resistant gram-negative organisms.

During the third week of ICU hospitalization, the patient continued to demonstrate respiratory deterioration despite ongoing supportive management. Oxygenation indices worsened and ventilatory requirements increased, suggesting progression of the underlying pulmonary pathology. The persistence of fever, combined with the radiologic progression of diffuse infiltrates on portable chest X-ray, reinforced the suspicion of a severe lower respiratory tract infection associated with prolonged critical care exposure.

At approximately 21 days of ICU stay, the clinical picture was highly suggestive of a healthcare-associated pulmonary infection complicating the patient's prolonged ventilatory course. Given the limitations of empirical diagnostic approaches and the need for precise microbiological identification, the decision was made to perform fiberoptic bronchoscopy with bronchoalveolar lavage (BAL) in order to obtain targeted lower respiratory tract samples for microbiological analysis. This procedure allowed direct visualization of the bronchial tree and facilitated the collection of distal airway secretions for culture and molecular diagnostic evaluation. (figure 3)

Figure 3

Clinical course of a 52-year old ICU patient developing ventilator-associated pneumonia caused by multidrug-resistant Klebsiella pneumoniae



The bronchoscopy findings revealed abundant purulent secretions within the bronchial tree, accompanied by marked mucosal inflammation and airway erythema, findings compatible with severe infectious involvement of the lower respiratory tract. Samples obtained through bronchoalveolar lavage were subsequently sent for microbiological culture and complementary diagnostic testing. The diagnostic process ultimately confirmed infection by multidrug-resistant *Klebsiella pneumoniae*, representing a major infectious complication acquired during the prolonged ICU stay.

This clinical trajectory illustrates the progressive evolution from initial severe respiratory failure to a complex ICU-acquired pulmonary infection, highlighting the critical role of prolonged mechanical ventilation, invasive airway instrumentation, and extended hospitalization in the emergence of multidrug-resistant pathogens in critically ill patients.

Diagnostic assessment

The suspicion of a secondary infectious process arose progressively during the patient's prolonged ICU stay as new clinical, radiological, and laboratory findings emerged that could not be explained solely by the initial respiratory condition. During the third week of hospitalization, the patient developed persistent febrile episodes accompanied by increased tracheobronchial secretions and worsening respiratory parameters. These changes occurred in the context of prolonged invasive mechanical ventilation, a well-recognized risk factor for healthcare-associated lower respiratory tract infections.

From a clinical standpoint, the patient exhibited several features suggestive of ventilator-associated pneumonia or ICU-acquired pulmonary infection. The appearance of purulent airway secretions, persistent systemic inflammatory response, and a progressive decline in oxygenation raised concern for an evolving infectious process. Ventilatory requirements increased during this phase, and oxygenation indices worsened despite ongoing supportive management, suggesting progression of pulmonary pathology rather than simple delayed recovery from the initial respiratory insult.

Radiological assessment provided additional support for this suspicion. Serial portable chest radiographs demonstrated the presence of diffuse bilateral pulmonary infiltrates with progressive radiological worsening over time. These findings were consistent with an inflammatory or infectious pulmonary process and correlated with the patient's deteriorating respiratory mechanics. The radiographic pattern suggested the possibility of severe lower respiratory tract infection complicating the patient's critical care course.

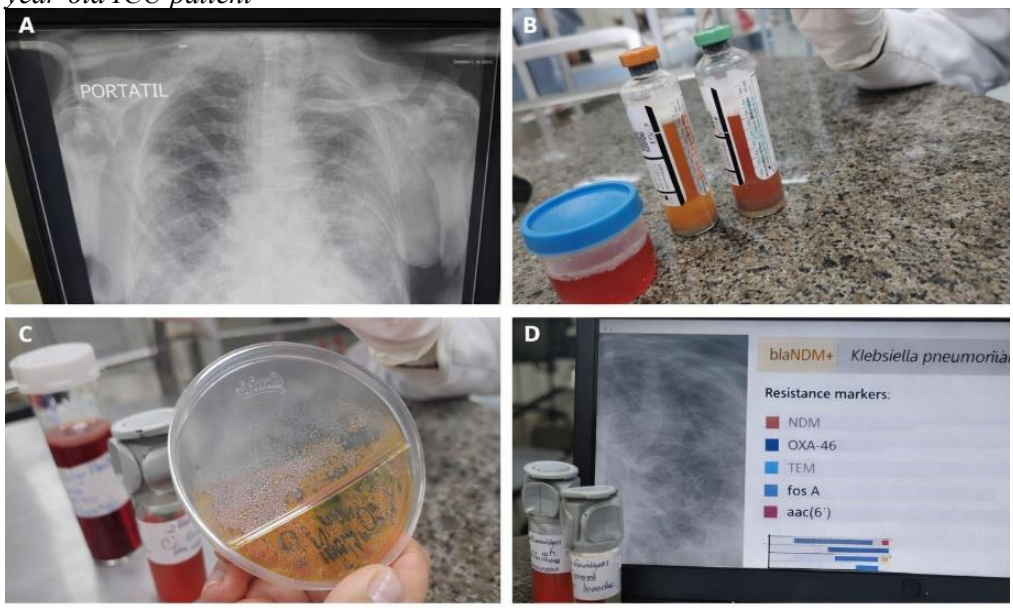
Laboratory evaluation further reinforced the suspicion of infection. The patient demonstrated inflammatory markers compatible with an ongoing systemic inflammatory response, including leukocytosis and elevated acute phase reactants. However, despite the clinical suspicion of infection, the precise microbiological etiology could not be established through routine initial investigations. Early microbiological cultures did not provide definitive diagnostic information, and empirical antimicrobial therapy had been initiated based on clinical criteria given the patient's critical condition and the high risk associated with delayed treatment. Because of the persistent clinical deterioration and the absence of clear microbiological identification, the medical team decided to pursue a more targeted diagnostic approach. Fiberoptic bronchoscopy was performed in order to directly evaluate the lower respiratory tract and obtain protected respiratory samples. During bronchoscopic evaluation, the bronchial tree showed marked mucosal

inflammation with abundant purulent secretions obstructing several airway segments, findings strongly suggestive of severe infectious involvement.

Bronchoalveolar lavage (BAL) was subsequently performed during the procedure to obtain distal airway samples for microbiological analysis. The BAL fluid was sent for culture and sensitivity testing in order to identify the responsible pathogen and guide antimicrobial therapy. Microbiological culture of the BAL sample later revealed the presence of *Klebsiella pneumoniae* with a multidrug-resistant phenotype. Given the diagnostic limitations present in the hospital setting and the clinical severity of the case, the patient's relatives sought complementary diagnostic testing through a private laboratory. A multiplex molecular assay was performed on respiratory samples to further characterize the infectious agent and its resistance mechanisms. The molecular analysis confirmed the presence of *Klebsiella pneumoniae* harboring resistance determinants compatible with New Delhi metallo-β-lactamase (NDM) production, thereby establishing the diagnosis of NDM-producing multidrug-resistant *Klebsiella pneumoniae* infection. (figure 4).

Figure 4

Diagnostic assessment that led to the detection of NDM-MDR Klebsiella pneumoniae in a 52-year-old ICU patient



(A) Chest X-ray showing bilateral pulmonary infiltrates. (B) Bronchoalveolar lavage (BAL) fluid samples. (C) Culture showing growth of NDM-MDR *Klebsiella pneumoniae*. (D) Multiplex assay results identifying blaNDM-positive *Klebsiella pneumoniae* with resistance markers.

The integration of clinical findings, radiological progression, bronchoscopy results, BAL culture, and complementary multiplex molecular testing ultimately allowed a definitive etiological diagnosis. This case highlights the diagnostic challenges frequently encountered in resource-limited hospitals, where delayed microbiological identification may occur and where complementary diagnostic support—sometimes facilitated by patients' families—can play a crucial role in clarifying complex infectious processes in critically ill patients.

Therapeutic intervention

Initial management in the ICU was directed toward stabilization of acute hypoxemic respiratory failure and prevention of further organ dysfunction. The patient was placed on invasive mechanical ventilation using a lung-protective strategy, with adjustment of tidal volume, positive end-expiratory pressure, and inspired oxygen fraction according to serial gasometric and clinical response. Supportive critical care measures included continuous hemodynamic monitoring, sedation and analgesia titration, airway clearance, fluid balance optimization, thromboprophylaxis, stress ulcer prophylaxis, nutritional support, and close surveillance for ICU-related complications. Because the initial presentation was compatible with severe pulmonary infection in a critically ill host, empirical broad-spectrum antimicrobial therapy was started early, aiming to cover the most likely community-acquired or early hospital-acquired respiratory pathogens while taking into account the epidemiological context and the patient's comorbid burden.

As the ICU course progressed, therapeutic decisions were repeatedly reassessed in response to persistent ventilatory dependence, progressive radiological infiltrates, fever, and increasing tracheobronchial secretions. The antimicrobial regimen was modified according to the evolving clinical picture and the growing suspicion of a healthcare-associated lower respiratory tract infection. At this stage, escalation of empirical therapy was driven not only by the persistence of systemic inflammatory signs but also by the high pretest probability of ventilator-associated pneumonia caused by multidrug-resistant gram-negative organisms, given the prolonged ICU stay and extended exposure to invasive airway support. In parallel, general ICU support was maintained and optimized, including repeated ventilatory adjustments, bronchial hygiene, and management of secretion burden.

A decisive therapeutic turning point occurred after fiberoptic bronchoscopy and bronchoalveolar lavage were performed. The presence of abundant purulent secretions and inflamed bronchial mucosa supported the clinical impression of severe lower respiratory tract infection, but the key value of the procedure was that it allowed acquisition of distal respiratory samples for targeted microbiological assessment. Once BAL culture identified multidrug-resistant *Klebsiella pneumoniae*, and complementary private multiplex testing confirmed the presence of NDM-associated resistance, antimicrobial management shifted from broad empirical coverage to a more focused and microbiologically informed strategy. This transition was essential because it allowed therapeutic decisions to be aligned with the pathogen's resistance profile rather than with syndromic suspicion alone.

In practical terms, antimicrobial adjustment was guided by three core principles: first, discontinuation of ineffective or insufficiently active empirical agents; second, prioritization of agents with the greatest expected activity against the documented multidrug-resistant phenotype; and third, adaptation of the final regimen to local drug availability in a resource-limited hospital

setting. This last point was particularly relevant in the present case, since the ideal evidence-based options for carbapenem-resistant or NDM-producing Enterobacterales are not always immediately accessible in secondary-level institutions. Therefore, the therapeutic approach required a balance between microbiological rationality, drug access, and the patient's dynamic clinical status.

Beyond antimicrobial therapy, ICU support remained central to treatment success. The patient required continued ventilatory management, strict monitoring of oxygenation and respiratory mechanics, serial imaging follow-up, and ongoing multidisciplinary care. Bronchial secretion control, prevention of ventilator-associated complications, and supportive care targeting organ preservation were maintained throughout this period. Treatment response was assessed through integrated clinical parameters, including fever curve, oxygenation, ventilatory requirements, secretion characteristics, inflammatory markers, and radiological progression.

Following antimicrobial optimization and continued critical care support, the patient showed partial clinical response, with reduction in infectious burden indicators and gradual stabilization of respiratory status. Although recovery was not immediate, the targeted approach improved therapeutic direction and reduced diagnostic uncertainty. This phase of the case illustrates that, in critically ill patients with prolonged ICU exposure, effective intervention depends less on indiscriminate antibiotic escalation and more on timely transition from empirical therapy to targeted treatment based on bronchoscopy, BAL culture, and molecular resistance characterization. In that sense, the therapeutic logic of this case was built on progressive refinement: early empirical coverage for a life-threatening syndrome, escalation during clinical deterioration, and microbiologically guided adjustment once the true pathogen and resistance mechanism were identified.

Outcome and follow-up

Following microbiologically guided adjustment of antimicrobial therapy and continuation of comprehensive ICU support, the patient entered a phase of gradual clinical stabilization. The immediate objective after confirmation of multidrug-resistant NDM-producing *Klebsiella pneumoniae* was to control the infectious process while preventing further deterioration in respiratory and systemic function. In the days after therapeutic optimization, the patient showed partial improvement in the main indicators of infectious and respiratory burden. Febrile episodes became less frequent, the volume and purulence of airway secretions decreased, and inflammatory parameters showed a progressive downward trend, suggesting at least partial control of the lower respiratory tract infection.

From a respiratory perspective, the patient remained critically dependent on ventilatory support during the early post-diagnostic period, but ventilatory requirements gradually became more stable. Serial assessment showed less pronounced deterioration in oxygenation, and subsequent clinical monitoring suggested a slow but favorable response in pulmonary mechanics.

This evolution was particularly relevant given the severity of the initial respiratory failure and the superimposed ICU-acquired multidrug-resistant infection. Repeated radiographic evaluation continued to show bilateral pulmonary involvement, although the pattern became more consistent with a slowly resolving inflammatory process rather than uncontrolled progression.

The overall clinical response was not immediate, which is expected in critically ill patients with prolonged ICU exposure and severe multidrug-resistant pneumonia. Instead, recovery followed a stepwise course marked by cautious improvement rather than abrupt reversal. Ongoing ICU measures remained essential throughout this phase, including ventilatory adjustment, secretion management, nutritional support, prevention of secondary complications, and multidisciplinary surveillance. These interventions helped sustain organ function while antimicrobial therapy exerted its effect against the documented pathogen.

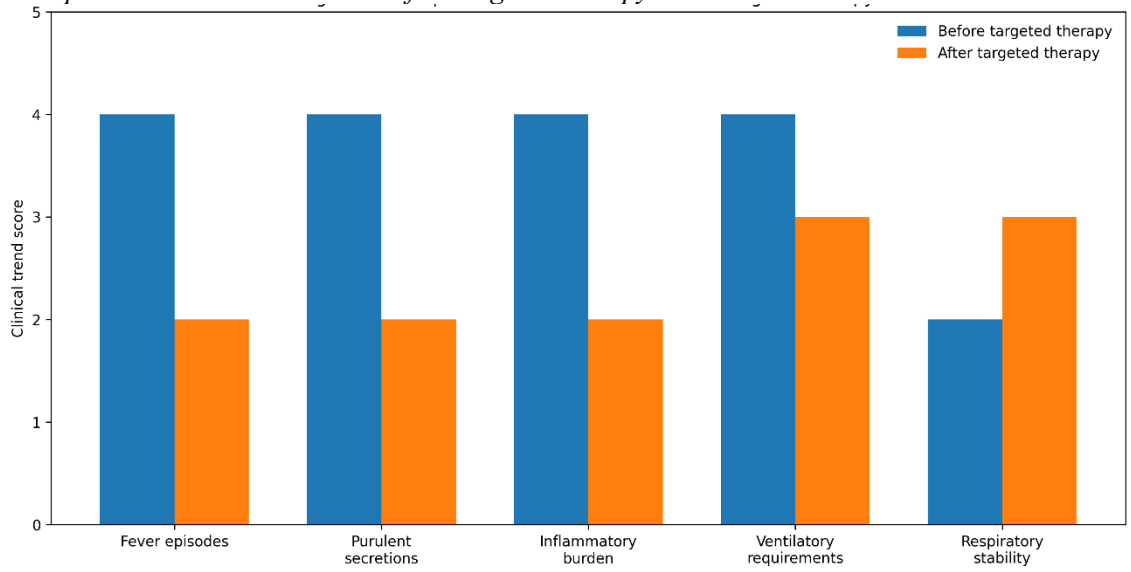
Follow-up after etiological confirmation also served an important stewardship function. Once the causative organism and resistance profile had been established, treatment could be maintained with greater precision, reducing the uncertainty associated with prolonged empirical escalation. This allowed the medical team to align subsequent decisions with the patient's real microbiological diagnosis and to better assess therapeutic response using targeted clinical and laboratory markers.

Although the case was characterized by high complexity, prolonged hospitalization, and significant infectious burden, the diagnostic clarification obtained through bronchoscopy, bronchoalveolar lavage culture, and complementary multiplex testing meaningfully changed the clinical trajectory. It transformed the case from one of persistent unresolved pulmonary deterioration into a defined multidrug-resistant infectious syndrome with a directed therapeutic pathway. In that sense, the follow-up period confirmed the value of accurate microbiological identification in critically ill patients, particularly in resource-limited settings where delayed diagnosis may prolong ineffective treatment and worsen outcomes.

This case therefore illustrates an outcome shaped not only by the virulence and resistance profile of the pathogen, but also by the timing of diagnostic precision. The patient's subsequent course supports the concept that, even in severe ICU-acquired infections caused by multidrug-resistant organisms, clinically meaningful stabilization may be achieved when microbiological diagnosis, antimicrobial adjustment, and sustained critical care support converge in a timely and coordinated manner.

Figure 5

Semiquantitative outcome trends after targeted therapy



Schematic bar chart based on narrative outcome data. Replace with actual follow-up values if available.

DISCUSSION

This case illustrates a clinically relevant and increasingly frequent scenario in critical care: the transition from severe primary respiratory failure to a complex ICU-acquired lower respiratory tract infection caused by multidrug-resistant *Klebsiella pneumoniae*. Its importance lies not only in the microbiological finding itself, but in the sequence through which the diagnosis emerged. The patient entered the ICU with severe hypoxemic respiratory failure and substantial baseline vulnerability. However, the later appearance of fever, progressive infiltrates, purulent secretions, and worsening ventilatory requirements shifted the clinical picture toward a superimposed nosocomial infection, highlighting the dynamic nature of pulmonary deterioration in prolonged ICU stays.

One of the main lessons of this case is that prolonged invasive mechanical ventilation remains a major epidemiological and pathophysiological driver of secondary infection. In critically ill patients, persistent airway instrumentation, impaired mucociliary clearance, repeated secretion retention, and sustained exposure to hospital flora create the ideal conditions for colonization and subsequent infection by resistant gram-negative organisms. In this context, *Klebsiella pneumoniae* is particularly concerning because of its virulence, adaptive capacity, and frequent association with carbapenem resistance mechanisms such as NDM production. Once these resistance patterns emerge, therapeutic options become narrower and the margin for empirical error becomes dangerously small.

Another relevant aspect is the diagnostic delay. In many secondary-level hospitals, routine microbiological workup may be insufficient to promptly identify the causative pathogen or its resistance determinants. This was evident in the present case, where early diagnostic approaches

did not fully clarify the etiology. Bronchoscopy with bronchoalveolar lavage became a decisive step because it allowed direct visualization of the bronchial tree and collection of distal respiratory samples, improving diagnostic precision beyond syndromic suspicion alone. The subsequent BAL culture confirmed multidrug-resistant *Klebsiella pneumoniae*, while the privately funded multiplex study obtained by the family contributed crucial information by identifying NDM-associated resistance. This detail reflects a common reality in resource-limited Latin American settings, where families sometimes become active facilitators of advanced diagnostics that are not readily available within the institution.

From a therapeutic standpoint, the case reinforces that successful management in critical care depends less on indiscriminate antibiotic escalation and more on timely movement from empirical treatment to microbiologically guided therapy. The value of the diagnostic process was not merely descriptive; it directly changed the therapeutic trajectory by allowing alignment between antimicrobial selection and the actual resistance profile.

Overall, this case underscores three central messages: first, prolonged ICU exposure should raise early suspicion for multidrug-resistant pulmonary infection; second, bronchoscopy with BAL remains highly valuable when conventional evaluation is inconclusive; and third, strengthening microbiological capacity and antimicrobial stewardship in resource-limited hospitals is essential to improve outcomes in critically ill patients with complex healthcare-associated infections.

CONCLUSION

This case highlights the clinical and microbiological complexity of ICU-acquired lower respiratory tract infections in patients with prolonged critical illness, invasive mechanical ventilation, and significant baseline comorbidities. What initially presented as severe acute respiratory failure evolved into a more intricate infectious process that could not be fully explained by the primary pulmonary insult alone. The subsequent appearance of persistent fever, progressive bilateral infiltrates, increased purulent airway secretions, and worsening ventilatory requirements strongly suggested a superimposed healthcare-associated infection, emphasizing the need for continuous reassessment in patients with prolonged ICU exposure.

A central conclusion from this report is that the diagnosis of multidrug-resistant pulmonary infection in critical care often requires progression beyond routine empirical reasoning. In this patient, conventional clinical and radiological suspicion was necessary but not sufficient. The decisive diagnostic turning point was achieved through fiberoptic bronchoscopy with bronchoalveolar lavage, which enabled direct assessment of the lower respiratory tract and collection of microbiologically meaningful distal airway samples. The identification of multidrug-resistant *Klebsiella pneumoniae* in BAL culture, followed by confirmation of NDM-associated resistance through complementary multiplex testing, transformed a nonspecific picture

of persistent respiratory deterioration into a defined etiological diagnosis with direct therapeutic implications.

This case also underscores a broader structural reality: in resource-limited secondary-level hospitals, diagnostic delays are often not caused by lack of clinical suspicion, but by restricted access to advanced microbiological tools. In such settings, decisions are frequently made under uncertainty, and families may become unexpected but important facilitators of complementary diagnostic support. Although this reflects inequity in access, it also demonstrates the practical value of molecular tools in clarifying resistant infectious syndromes when conventional methods are delayed or inconclusive.

From a clinical standpoint, the case supports an approach based on progressive refinement rather than indiscriminate therapeutic escalation. Early empirical antimicrobial coverage was justified by the severity of the syndrome, but meaningful improvement required transition to microbiologically guided treatment once the pathogen and resistance mechanism were identified. This reinforces the importance of integrating invasive respiratory sampling, targeted microbiology, and antimicrobial stewardship into ICU decision-making.

Ultimately, this report shows that multidrug-resistant NDM-producing *Klebsiella pneumoniae* should be considered a major threat in prolonged ICU admissions, particularly in mechanically ventilated patients with unresolved pulmonary deterioration. Early suspicion, timely bronchoscopy with BAL, improved microbiological capacity, and rational antimicrobial adjustment are essential pillars for improving diagnostic precision and therapeutic effectiveness in critically ill patients managed in constrained healthcare environments.

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