Molecular diagnosis of polymicrobial sepsis in pediatric patient: a case report

Diagnóstico molecular de sepsis polimicrobiana en paciente pediátrico: reporte de un caso

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Abstract

Polymicrobial sepsis is a controversial diagnosis, being feasible in patients with a history of surgical interventions, and abdominal sepsis, among other risk factors. The case of a pediatric patient with multiple hospitalizations and surgical interventions due to an underlying diagnosis of type IV multiple jejunal atresia that produced polymicrobial sepsis confirmed by molecular biology and traditional cultures is described below. It is important to consider polymicrobial sepsis in blood cultures taken with the correct technique, since the identification of pathogens leads to targeted treatment, increasing the probability of survival of these patients.

El diagnóstico de sepsis polimicrobiana es controvertido, se ha considerado factible en pacientes con antecedentes de intervenciones quirúrgicas, sepsis abdominal, entre otros factores de riesgo. A continuación, se describe el caso de un paciente pediátrico con múltiples hospitalizaciones e intervenciones quirúrgicas por el diagnóstico de base de atresia yeyunal múltiple tipo IV que produjo sepsis polimicrobiana confirmada por biología molecular y cultivos tradicionales. Es importante considerar la sepsis polimicrobiana en hemocultivos tomados con la técnica correcta, ya que la identificación de patógenos conduce al tratamiento dirigido, aumentando la probabilidad de supervivencia de estos pacientes.


Introduction

Confirmed polymicrobial sepsis is rare in pediatrics and is associated with factors such as underlying medical conditions, gastrointestinal problems, malignancies, or a central venous access device 1-4. Thus, here we present a rare case of a pediatric patient with sepsis with abdominal focus with molecular and phenotypic detection of Acinetobacter baumannii, Klebsiella pneumoniae producing serinecarbapenemase (KPC), Enterococcus faecalis, and Staphylococcus epidermidis MRSA and constitutive MLSb.

Case report

An 11-month-old infant, the product of the first pregnancy of an adolescent mother (16 years old), whose pregnancy was uneventful. This patient was born by cephalo-vaginal delivery, APGAR 9 at 1 minute and APGAR 10 at 5 minutes of life, and anthropometric measurements within normal limits. Initially, on examination, the patient’s general condition was good.

There was no obvious congenital anomaly, later in the neonatology room, the patient presented bilious vomiting 12-15 episodes/24 hours in the absence of abdominal distension.

For this clinical presentation, abdominal radiography and ultrasonography were requested and showed dilated small bowel loops. This patient received a diagnosis of intestinal atresia and was transferred to a third-level pediatric hospital, where an exploratory laparotomy was performed, which confirmed multiple type IV jejunal atresia, for which a proximal end resection + ileostomy was performed.

After this, the patient was hospitalized on 2 previous occasions in the same hospital, due to diarrhea, severe dehydration, and malnutrition. At 7 months of age, he presented with sepsis of an abdominal focus, secondary to a procedure to restore intestinal transit, and received a non-detailed broad-spectrum antibiotic treatment.

At 10 months of age on February 20, 2019, he was admitted to a third-level public hospital. He was admitted for new sepsis of abdominal focus, pneumonia, urinary tract infection (UTI) by E. coli and Candida sp., hydro electrolytic disorder, chronic malnutrition, and cardiorespiratory arrest on 2 occasions.

For the management of his infectious etiologies, this patient was treated with:

- ampicillin (200 mg/kg/day),
- amikacin (15 mg/Kg/day),
- metronidazole (30 mg/Kg/dose),
- fluconazole (6 mg/Kg/dose),
- ceftriaxone (40 mg/Kg/day),
- linezolid and meropenem (40 mg/Kg/day).

During this condition, he remained hospitalized for 29 days and was discharged due to a favorable evolution.

Ten days later he went to a different pediatric hospital with 10 months and 28 days of life. He was admitted to the emergency room with a clinical history of 12 hours, characterized by: vomiting, hyporexia, and decay.

On physical examination: the patient was asthenic, irritable, pale, crying without tears, with cold skin and dry oral mucous membranes, sunken eyes, moderate nasal discharge, capillary filling for 3 seconds, abdomen with increased air-fluid noises, ileostomy sheath with 20 mL of fecal fluid content.
For this reason, he was admitted with a diagnosis of moderate dehydration, protein-calorie malnutrition, ileostomy carrier, fluid and electrolyte disorder, prerenal renal failure, and oral candidiasis. In an emergency, dehydration and electrolyte imbalance were immediately corrected.

On the same day, antibiotic therapy was started with ceftriaxone at 100 mg/kg/day and they were impregnated with fluconazole at 6 mg/kg due to their history of previous fungal infection.

Patient with apparent clinical improvement, however, on the seventh day of hospitalization, presented temperature increase with the presence of leukocytes of 18,000/mm3, C-reactive protein of 500 mg/dL, procalcitonin of 14 ng/dL, 2 new peripheral blood cultures were taken under aseptic conditions and empirically covered for Gram positives with vancomycin at 45 mg/Kg/day.

At 6 hours after incubation in semi-automated equipment for blood cultures (BD Bactec Fx 40) the two bottles were positive, and gram-negative bacilli were observed in the stain. Due to the torpid evolution of this patient, real-time multiplex PCR was performed for sepsis using the BioFire FilmArray blood culture panel (BioFire Diagnostics LLC, Salt Lake City, UT).

In the blood culture panel for sepsis, genes were detected of Acinetobacter baumannii, Klebsiella pneumoniae resistance gene KPC, Enterococcus, Staphylococcus mecA resistance gene (Figure 1).

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Subsequently, in cultures, microbiology reported: Acinetobacter baumannii, Klebsiella pneumoniae producer of serinecarbapenemases with susceptibility to colistin, Enterococcus faecalis, and Staphylococcus epidermidis resistant to cefoxitin and constitutive MLSb (Figure 2).

Therefore, the pediatric infectious disease specialist established intravenous treatment for 14 days with colistin

- (activity of 15 colistin base (AUC)/kg/day),
- and amikacin (20 mg/kg/day),
- meropenem (40 mg/kg/day). dose every 8 hours
- and vancomycin (40 mg/Kg/day).
- The patient remained stable during his 14 days of intravenous antibiotics.

Based on the pediatric infectious disease request by the criterion that repeating blood cultures may increase the diagnostic yield for conditions such as infective endocarditis and may have implications for the duration of antibiotic therapy, two peripheral blood cultures were performed under aseptic conditions on the fifth day of antibiotic therapy, which were negative.

After arduous management by a multidisciplinary team, the patient was discharged, having overcome his polymicrobial sepsis of abdominal origin after 32 days of hospitalization.

Sepsis has a worldwide relevance in all ages, risk factors include the extremes of age, abdominal comorbidities, abdominal surgeries, etc.

Thus, the case analyzed presented a sum of these risk factors characterized by age, congenital jejunal atresia, multiple abdominal interventions, and malnutrition. In addition, the multiple hospitalizations predisposed this patient even to infections associated with health services

It is important to mention that initially the patient was treated in another hospital for his surgical needs, where he received various cycles of broad-spectrum antibiotics. Unfortunately, it was not possible to obtain a detailed history of which antibiotics, dosage, and the number of cycles he had previously received. This background is crucial because it disrupts the gut microbiome and increasingly recognized modulator of the immune system and outcomes in sepsis.

Previously, there was the criterion that an infection could be produced only by a pathogen supported by Koch’s postulates, but currently, it has been shown that infections can be polymicrobial as in the case presented, being important to highlight that the multiple hospitalizations where he received several antibiotics of different spectra made the traditional microbiological diagnosis difficult.

The use of antibiotics tends to inhibit the growth of infection-producing pathogens in artificial cultures. Because the therapeutic spectrum was reduced in the emergency of the last hospitalization to ceftriaxone and fluconazole, a window was produced where the diagnosis was achieved by traditional and molecular microbiology.

In septic patients, the culture of blood, urine, cerebrospinal fluid, or other tissues is essential to detect infection. Microbiological analysis is the gold standard despite its limitations regarding response time and the ability to detect only culturable pathogens.

In this way, molecular methods can shorten the identification time helping to establish therapies based on the microorganisms detected and their resistance mechanisms, if any, thus there is a methodology with multiplex PCR (Polymerase Chain Reaction) in real-time that allows the detection of several pathogens in a simultaneous test that even contain
resistance genes such as MRSA, KPC, VAN A for the most frequent resistance mechanisms, which are a very helpful tool in polymicrobial sepsis 5,6.8.

Usually, whenever more than two pathogens are detected in blood cultures, contamination is suspected. Therefore, the diagnosis of polymicrobial sepsis is controversial.

The detection of real cases in pediatrics is rare and is associated with factors such as underlying medical conditions, patients with gastrointestinal problems, malignancies, or a central venous access device 3-5.

In this patient, a sum of criteria supported sepsis as polymicrobial, such as leukocytosis, increased C reactive protein, increased procalcitonin, and fever. The advantage of molecular microbiology is that it searches for sequences of the pathogen’s genetic material as well as resistance genes that have an important impact on therapeutics. Based on the long-standing clinical history, with previous hospitalizations, multidrug-resistant pathogens of hospital origin were suspected, so multiplex real-time PCR was recommended for sepsis.

This allowed, in 7 hours after taking 2 peripheral blood cultures in sterile conditions, to cover with antibiotics that improved the spectrum such as amikacin and colistin.

The association of meropenem, amikacin, colistin, and vancomycin had a good clinical course in this patient. Based on what has been discussed, it is essential to analyze all risk factors in pediatric patients with previous hospitalizations, it is important to suspect multidrug-resistant pathogens, especially if there is a history of previous infections, the use of broad-spectrum antibiotics, invasive devices, and long-term hospitalization.

There are new diagnostic tools that allow us to detect pathogens in sepsis and medical scientific evidence recommends the use of these as they can directly influence antibiotic therapy and patient survival, especially in patients with septic shock where the establishment of an early effective antibiotic therapy decreases the risk of mortality 1,4,6.

Conclusions

It is essential to individually evaluate each patient who has criteria for sepsis with special attention to risk factors as they will allow a more focused diagnosis and management. The blood culture collection technique in septic patients is essential to ensure the reliability of the results, especially in those cases where there are risk factors for polymicrobial sepsis 11.

In patients hospitalized for more than 3 days or with a history of previous hospitalizations in the last month, there is the possibility of infections by nosocomial microorganisms, and this can represent a challenge for diagnosis and antimicrobial therapy 12.

Although traditional blood cultures continue to be the gold standard, it is interesting to consider the new molecular diagnostic tools that can shorten waiting times for results and can help guide initial antimicrobial therapy. Despite this, traditional cultures are essential since they are the only ones that can show the results of bacterial susceptibility to different antibiotics.

On the other hand, molecular techniques for the syndromic diagnosis of sepsis with panels that detect several microorganisms are more susceptible to detecting false positives, for which these results must always be correlated with the clinical status of each patient, and it is also important to know that only is possible apply these panels in positive blood cultures 13-15.

Special attention should be paid to pediatric patients because their management is different from adults. An example of this is the dose of antibiotics, which must be adjusted to various factors, such as weight 16.

Recommendations

Specialized management by pediatricians with training in pediatric sepsis management or subspecialists in pediatric infectious disease is recommended for this type of patient 16.

It is always necessary to request cultures in pediatric patients with sepsis since this can help us identify the site of infection, the pathogen, and its resistance mechanisms that directly impact the choice of antimicrobial 16,17.

There is an urgent need to train laboratory personnel and physicians in the new diagnostic techniques in sepsis since they can improve survival after an early diagnosis.
It is critical to adjust the dose of antibiotics in pediatrics to weight, since many patients may have changed during hospitalization, also to preserve renal and hepatic function 18.

If antimicrobial therapy has no clinical effect after 72 hours of administration, it is important to consider whether the dose is correct, whether other drugs are interfering with the antibiotics, whether the site of infection and my chosen drug have adequate penetrance, whether the nursing staff is carrying out a correct dilution and administration of the medication, and in cases that warrant, multi-resistant microorganisms should be considered and the therapy should be escalated based on the epidemiology or the microbiological surveillance chart of your hospital 19.

Finally, it is essential to have a doctor or laboratory personnel with training in medical microbiology with a clinical approach, which can be a great help for clinicians who, in case of doubts or difficulties in the microbiological diagnosis of sepsis, can consult with personnel trained in the subject 20-23.

Conflicts of Interest: The authors declare no conflict of interest.

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Reference


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