A FATAL CASE OF LISTERIOSIS IN A PAEDIATRIC RENAL TRANSPLANT PATIENT

MIRTINAS VAIKO LISTERIOZĖS ATVEJIS PO INKSTO TRANSPLANTACIJOS

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SANTRAUKA

Reikšminiai žodžiai: listeriozė, meningitas, vaikai, inkstų transplantacija, imunosupresija.


ABSTRACT

Key words: listeriosis, meningitis, paediatric, renal transplantation, immunosuppression.

Listeriosis is a rare but highly fatal opportunistic foodborne infection caused by the aerobic, gram-positive intracellular pathogen Listeria monocytogenes. Invasive forms of listeriosis are associated with a very high fatality rate, and include bacteremia, central nervous system infection, materno-fetal and focal infections. We present a case of a 12-year-old girl with a history of renal transplantation and a year of immunosuppressive therapy who developed invasive listeriosis after the consumption of unpasteurized milk. The initial diagnosis of listeriosis was challenging and required extensive testing to exclude other possible causes of diarrhea, pyrexia and deteriorating renal function. Sepsis and meningitis developed and eventually our patient died despite adequate antibiotic therapy with ampicillin and meropenem.

INTRODUCTION

Listeriosis is a highly fatal opportunistic foodborne infection predominantly affecting people with impaired cell-mediated immunity [1, 2]. It is caused by an aerobic, gram-positive intracellular pathogen Listeria monocytogenes commonly found in raw and unprocessed food products [3]. Moreover, Listeria monocytogenes is characterised by the ability to cross various barriers, including the placenta, intestinal mucosa and blood-brain barrier [4]. Listeriosis is a rare disease with an estimated annual incidence of 3.3 cases per million in the U.S. population [5]. Groups primarily affected include pregnant women, newborns, the elderly, transplant recipients and other immunocompromised individuals [6, 7, 8]. Clinical manifestations of listeriosis range from febrile gastroenteritis and localized infections to life-threatening invasive forms such as endocarditis, central nervous system infections, sepsis, perinatal infections and miscarriages [8, 9]. An antibiotic regimen is crucial in the treatment of listeriosis, however, the mortality rate is 20 % to 40 % despite the adequate therapy [2, 4]. Although listeriosis following organ transplantation has been well-des-
scribed in the literature, clinical manifestation in paediatric renal transplant patients remains scarcely documented. We encountered a case of fatal *Listeria monocytogenes* infection in a 12-year-old girl with a history of renal transplantation and one year of immunosuppressive therapy.

**CASE REPORT**

At the age of two years, the patient was diagnosed with bilateral vesicoureteral reflux of 3rd grade, recurrent pyelonephritis and bilateral nephrosclerosis. Eventually, end-stage kidney disease developed and at the age of 10 years a deceased donor kidney was transplanted. The patient was started on an immunosuppressive regimen that included basiliximab (20 mg before and on the 4th day after operation); cyclosporine (125 mg twice daily); mycophenolate (1 g twice daily) and methylprednisolone (4 mg twice daily) and afterwards maintained on cyclosporine (125 mg twice daily); mycophenolate (750 mg twice daily); and prednisone (10 mg daily) (Fig. 1). The patient had frequent infections: subclavian vein catheter infection; recurrent urinary tract infection; and vulvitis. At five months post-transplantation, kidney function worsened and acute rejection was diagnosed. Doses of immunosuppressive agents were adjusted and a regimen consisting of cyclosporine (50 mg twice daily), mycophenolate (750 mg twice daily) and prednisone (15 mg daily) was administered. However, 10 months after transplantation the patient was admitted to the hospital for abdominal pain, diarrhoea and frequent vomiting. Laboratory tests showed blood urea nitrogen (BUN) 22 mmol/l, serum creatinine 400 µmol/l with glomerular filtration rate 11 ml/min/1.73 m². Acute rejection was suspected and three intravenous pulses of methylprednisolone (250 mg) were administered followed by prednisone (2 mg/kg) p/o, but transplant function did not improve. A transplant biopsy showed type 2B acute rejection (Banff classification of rejection). Horse antithymocyte globulin (ATG) (250 mg daily) was administered. After the second dose, an acute allergic reaction developed and the medication was replaced with rabbit ATG (100 mg daily). After the 8th infusion of rabbit ATG, kidney function improved (BUN: 9.4 mmol/l, serum creatinine: 213 µmol/l), but anaemia developed (Hb: 67 g/l, RBC: 2.69 × 10¹²/l). Therefore, subcutaneous erythropoietin was administered and continued with regular immunosuppressive treatment plus prednisone (2 mg/kg/d). However, kidney function worsened again and cytomegalovirus infection was suspected. Serologic tests showed positive CMV IgG and low-level pp65 CMV antigenemia. Kidney function did not improve despite the additional treatment with ganciclovir. The patient spent five weeks at home due to family circumstances but was hospitalized again for diarrhoea and subfebrile fever on the 12th month post-transplantation. A stool-culture showed

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**Figure 1. The course of the disease**
Candida, Morganella and Citrobacter growth and antibio-
tic treatment with ceftriaxone was administered. Despite
the treatment, the general state of the patient continued
to deteriorate: vomiting, diarrhoea and pyrexia manifes-
ted, along with tonic-clonic seizures with sharp horizontal
and rotating nystagmus, and hiccups. Listeriosis was sus-
pected from her epidemiological history of having consu-
med unpasteurized milk. Blood cultures showed Listeria
Monocytogenes. Additionally, raised levels of inflammatory
markers were found in her blood (C-reactive protein: 403
ng/ml, procalcitonin > 10 ng/ml). Ampicillin was adminis-
tered and immunosuppressive treatment was discontinued,
but symptoms persisted. On the 3rd day, the ampicillin was
replaced with meropenem. However, pancytopenia devel-
oped, her neurological condition did not improve, and her
cardiopulmonary insufficiency progressed. On the 6th day
of antibiotic therapy, the patient died. Post-mortem results
of blood and cerebrospinal fluid (CSF) cultures confirmed
the diagnosis of Listeria monocytogenes infection.

DISCUSSION

Our case illustrates how devastating listeriosis can be
in children receiving immunosuppressive treatment. Gene-
 rally, human listeriosis is one of the most fatal foodborne
infections among high-risk populations with a high morta-
 lity rate despite adequate therapy [2, 4, 10]. Immunocom-
 promised individuals, including patients maintaining
immunosuppressive regimen, are particularly susceptible
to invasive listeriosis that predominantly manifests as bac-
teraemia and meningitis [5, 9]. Additionally, the level of
overall immunosuppression (including induction therapy,
maintenance therapy, and the treatment of acute rejection
episodes) is considered to be a more significant risk factor
for post-transplant infections, such as listeriosis, than the
use of a particular immunosuppressive agent [11].

In this case, the immunosuppressive therapy was prob-
ably not the sole factor that determined the course and
outcome of the patient’s disease. Organ transplantation and
dialysis are among conditions with the highest incidence of
listeriosis (> 5 per 100 000). Patients with such conditions
account for 43% of listeriosis cases and 55% of deaths cau-
 sed by this infection. In comparison, the population consid-
red not at risk accounts for 10% of listeriosis cases and only
2% of deaths. In addition, CNS involvement is a risk factor
independently associated with an increased risk of death [2].
L. monocytogenes infection is the most common cause of bac-
terial meningitis in patients with underlying neoplastic dis-
ease and in organ transplant recipients (especially renal). In
a retrospective review of 820 cases of central nervous system
listeriosis not associated with pregnancy or neonatal period,
hematologic malignancies and renal transplantation were the
two most common predisposing conditions [12].

Moreover, early suspicion and antibacterial therapy si-
gnificantly increases the chances of good outcomes in the
treatment of listeriosis [13, 14]. However, the initial dia-
gnosis of this infection might be challenging due to L. mo-
nocytogenes rare microbiologic features and inconspicuous
symptoms of listeriosis [15, 16]. Furthermore, the differen-
tial diagnosis of diarrhoea in immunocompromised patients
is particularly complicated due to a wide range of possible
causes, varying from infections to diarrhoea induced by in-
munosuppressive agents [17]. As mentioned above, listerio-
sis is a particularly rare infection. Also it is usually sporadic
and has a long incubation period (7-60 days) which makes
it even more difficult to suspect [5]. According to various
data sources, diagnosis of invasive listeriosis is best estab-
lished by blood or cerebrospinal fluid cultures [4, 18].

Ampicillin is the drug of choice in the treatment of
invasive listeriosis and meropenem is indicated in cases of
allergy to ampicillin or when it does not show adequate
effect. However, there is currently a lack of studies on anti-
bacterial treatment for listeriosis due to the low incidence
of this infection [19]. Additionally, although listeriosis is a
rare infection, it should be suspected in cases of sepsis or
meningitis in patients receiving immunosuppressive treat-
ment. Furthermore, the initial empirical therapy of bacte-
rial meningitis in this risk group should include antibiotics
against Listeria monocytogenes [7].

Finally, the prevention of listeriosis relies on food safety.
Unfortunately, the importance of this infection is not eno-
ugh acknowledged because it is very rare. In our case, the
patient developed invasive listeriosis after the consump-
tion of unpasteurized milk. Unpasteurized milk and soft cheese
made with unpasteurized milk are included in the list of
L. monocytogenes-associated foods, and dairies are associated
with approximately half of foodborne listeriosis outbreaks
in Europe [20, 21]. This indicates that more attention to
food safety education and high-risk groups messaging is ne-
necessary to prevent listeriosis [22].

In conclusion, we present an extremely rare case of
invasive listeriosis in a paediatric renal transplant patient.
Rare infections such as this are worth including in the diffe-
rential diagnosis of bacterial meningitis in high-risk groups,
especially after renal transplantation. Although the mortali-
ty rate of invasive listeriosis is high, early antibacterial the-
rapy significantly increases the chance of a good outcome.
Thus, the use of antibodies against L. monocytogenes should
be included in the empirical antibacterial regimen in high-
risk patients with symptoms of bacterial meningitis. Lis-
teriosis is a potentially fatal but curable infection with an
early initial diagnosis and implementation of an adequate
antibacterial therapy.
REFERENCES

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