



BACTERIUM WITH LEUCONOSTOC PSEUDOMESENTEROIDES

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Introduction. *Leuconostoc pseudomesenteroides* until recently was classified as a commensal microorganism, but from 1985 until now several sporadic cases of infection with this pathogen have been described in humans. Bacteremia with *Leuconostoc* spp. are increasingly reported. Unique cases of infection of other sites have also been described. Most often, these cases have been reported in patients with cancer, and are often considered opportunistic for acquired immunodeficiencies. However, several cases have also been reported in immunocompetent patients.

Material and methods. An analysis of the literature and the clinical case are presented here: an 11-month-old child with congenital malformation – rabbit lip, who had pneumonia 2 months before his admission to the Toma Ciorba Infectious Diseases Clinical Hospital.

Results. Meningococemia and meningitis were clinically established upon admission. A few days later the blood culture result was with *Leuconostoc pseudomesenteroides*. The etiological treatment was corrected and the sterile result of the blood culture was obtained. The child was released in a satisfactory condition.

Conclusions. The clinical case presented is the first case of infection with *Leuconostoc* spp. described in the Republic of Moldova. The correct choice of the etiological treatment allows the eradication of this pathogen.

Cuvinte cheie: *Leuconostoc pseudomesenteroides*, malformație congenitală, bacteriemie, Rezistent la Vancomycin, Amoxicilina Clavulanat.

BACTERIEMIE CU LEUCONOSTOC PSEUDOMESENTEROIDES

Introducere. *Leuconostoc pseudomesenteroides* până nu demult a fost catalogat drept microorganism comensal, însă din 1985 până în prezent au fost descrise câteva cazuri sporadice de infecție cu acest agent patogen la om. Bacteriemiiile cu *Leuconostoc* spp. sunt tot mai frecvent raportate. Au fost descrise cazuri unice de infectare și ale altor situsuri. Cel mai des, aceste cazuri au fost atestate la pacienții cu stări canceroase, fiind deseori apreciate drept oportuniste imunodeficiențelor dobândite. Însă, și la imunocompetenți au fost descrise câteva cazuri.

Material și metode. Este prezentat o analiză a literaturii și un caz clinic al unui copil de 11 luni cu malformație congenitală – cheloschizis (buza de iepure), suportând pneumonie cu 2 luni înainte de internare.

Rezultate. La internare au fost stabilite clinic meningococemia și meningita. Peste câteva zile rezultatul hemoculturii a permis identificarea de *Leuconostoc pseudomesenteroides*. A fost corectat tratamentul etiologic și obținut rezultatul steril al hemoculturii. Copilul a fost externat în stare satisfăcătoare.

Concluzii. Cazul clinic prezentat este primul caz de infecție cu *Leuconostoc* spp. descris în Republica Moldova. Alegerea corectă a tratamentului etiologic permite eradicarea acestui agent patogen.

L. – *Leuconostoc*; **spp.** – species; **CNS** – Central Nervous System; **PMSI** – Public Medical Sanitary Institution; **IDCH** – Infectious Diseases Clinical Hospital; **SpO₂** – peripheral blood oxygen saturation; **ESR** – erythrocyte sedimentation rate, **ALT** – alanine aminotransferase; **AST** – aspartate aminotransferase, **Anti-CMV-IgG** – Antibodies Immunoglobulin G to *Cytomegalovirus*, **Anti-CMV IgM** – Antibodies Immunoglobulin M to *Cytomegalovirus*, **HBsAg** – Hepatitis B surface antigen, **anti-HCVsum** – summary antibodies to the hepatitis C virus, **B/P** – blood pressure, **CSF** – cerebrospinal fluid.

INTRODUCTION

Streptococcus-like bacteria of the genus *L.* (*Leuconostoc*) were isolated in humans for the first time by Handwerger in the mid-80s of the last century. *Leuconostoc spp.* are facultative-anaerobic, gram-positive, catalase-negative, non-spore-forming, motile, heterofermentative cocci widely distributed in the environment, including soil and plants (1).

The genus *Leuconostoc* includes the “typical representative” *L. mesenteroides* and 8 “minor” species, including *L. pseudomesenteroides*. Members of the genus *Leuconostoc* are more of an economic importance, as they are used in the manufacture of dairy products and wine. The first suspected case of human infection with *Leuconostoc spp.* was recorded in 1985 (2). Until then, *Leuconostoc* species were considered non-pathogenic for humans. Since 1985, infections caused by *Leuconostoc* have been reported more frequently (3-5), becoming more and more important as opportunistic pathogens of immunodeficiency states (6-8). For example, a South Korean study describes 6 cases of bacteremia with *Leuconostoc* in patients over 60 years old, with aggravating underlying diseases. Within 30 days of the identification of the bacteria, four of these 6 patients died (9).

At the same time, cases have also been described in immunocompetent patients. For example, secondary infection with *Leuconostoc spp.* following the application of a patch with plant components on the wound of a patient with amputation (10), or purulent meningitis caused by *Leuconostoc spp.* in a previously healthy patient (4), or bacteremia with the same pathogen in an immunocompetent patient suffering from Chagas disease (11), etc.

Leuconostoc infections often occur in patients whose underlying diseases are treated with vancomycin (12, 14). There are described cases of isolation of *Leuconostoc spp.* from the blood of patients with malignant neoplasms and long-term catheterization, as well as from the removal

of infected wounds, in postoperative infections and in odontogenic abscesses (4, 12, 15-17). Pulmonary infection with *Leuconostoc* in a patient with lymphoma is also described (18). Xinfeng Lin and co-authors (19) in his paper associated hemophagocytic syndrome with *Leuconostoc pseudomesenteroides* infection in an adult patient.

Central Nervous System (CNS) infections caused by *Leuconostoc spp.* are extremely rare. Most often they are associated with a deficient immune field, such as, for example, purulent meningitis with *Leuconostoc spp.* in newborns (20, 21). A case of nosocomial meningitis caused by *Leuconostoc spp.* has been described in connection with the use of a catheter with an extraventricular drainage system due to the presence of a thalamic hematoma with ventricular extension (2). Ventriculitis and brain abscess have also been described in CNS infections with *Leuconostoc spp.* (22, 23).

Several cases of *L. mesenteroides* bacteremia associated with the use of oral dietary supplements for children have been reported (3). Other additional factors that predispose to infection are: prolonged treatment in the hospital, the use of devices that violate the integrity of the skin and mucous membranes (venous catheters, gastro- or tracheostomy, drainage fistulas), extensive surgical interventions, decreased intestinal barrier function, antibiotic therapy with drugs that are not sufficiently active against *Leuconostoc spp.* (3, 5-7, 24).

It must be recognized that infectious diseases caused by *Leuconostoc spp.* are rare. This is also due to the lack of practice of its isolation. *Leuconostoc spp.* can be taken into consideration only in the case of isolation from obviously sterile sources (blood, cerebrospinal fluid, peritoneal and joint fluids), observing all the rules of asepsis. If *Leuconostoc* is found in material with a high risk of external contamination (for example, in the wound exudate), its presence is significant

only if no other more virulent microorganisms are found or if *Leuconostoc* is isolated in large quantities in several analysis of the sampled material (5, 6).

The complexity of identifying the microorganism is associated with the similarity of some of its properties with other, more frequently detected bacteria – *pneumococci, streptococci and lactobacilli*. These similarities can cause misidentification (25). The natural resistance of *Leuconostoc spp.* to vancomycin allows its rapid differentiation from most other streptococcal bacteria, except *Pediococcus spp.* and certain vancomycin-resistant strains of Enterococci. At the same time, carrying out tests using leucine aminopeptidase and pyrrodonylarylamidase allows the differentiation of *Leuconostoc spp.* with *Pediococcus spp.* and vancomycin-resistant *Enterococci* (26). In recent years, automated microbiological analyzers have been successfully used to confirm *Leuconostoc* bacteremia (27).

Leuconostoc is one of the few Gram-positive bacteria, including *Pediococcus spp., Lactobacillus spp., Erysipelothrix, enterococci*, naturally resistant to glycopeptide antibiotics – vancomycin and teicoplanin. However, despite resistance to glycopeptides, *Leuconostoc spp.* is sensitive to most antibiotics active against *streptococci*. Thus, *Leuconostoc* is usually sensitive to penicillin, ampicillin, clindamycin, erythromycin and fosfomycin. Moderate activity is shown by imipenem, cephalosporins, tetracyclines and chloramphenicol (6, 25). Clinical data, extremely limited in number, indicate that apparently the antibiotics of choice for the treatment of infections caused by *Leuconostoc spp.* are penicillin and ampicillin (5, 25).

CASE PRESENTATION

Patient V.D., 11 months old, was admitted to PMSI IDCH “Toma Ciorba” on 05.01.2022. When the patient was admitted, the following anamnestic data were found:

- Heredo-collateral antecedents: born with a congenital malformation – rabbit lip with a defect of the hard and soft palate, at 39 weeks, weighing 2970 gr.; was abandoned by parents (disenfranchised).
- Medical history: underwent 2 facial surgeries, performed at PMSI “E. Cotaga”; in November-December 2021 – pneumonia; until

the age of 9 months showing retardation in physical development, not sitting on their own.

- Living conditions: being adopted, he lives in a family that takes care of him; sufficient nutrition (quantitative and qualitative).

Epidemiological anamnesis: in the adoptive family there are children who previously (December 2021 – January 2022) showed signs of acute respiratory infection with cough, rhinorrhea and pain in the pharynx.

The history of the disease: considered sick since 03.01.2022, when fever up to 39.0°C appeared, liquid stool 3 times a day, general weakness, lack of appetite. The child caregiver administered oral antipyretics. On 04.01.22 the caregiver noticed the appearance of a punctate rash on the left buttock. The liquid stool did not recur, but the fever remained up to 39.5°C. On 05.01.22 multiple punctate eruptions appeared on the lower limbs, the fever continued to persist. The child caregiver requested Urgent Medical Assistance, after which the child was hospitalized with suspicion of meningococcal infection at PMSI Ungheni District Hospital, where he was administered sol. Levomycetin 250 mg and Ringer infusion i/v 100 ml. On the same day, the child was transported to PMSI IDCH “Toma Ciorba” for diagnostic evaluation and treatment.

Clinical examination: serious general condition, body temperature – 37.4°C, drinks very little, with difficulty; punctate and stellate hemorrhagic eruptions located on the lower limbs and in the lower abdomen, two elements – on the buttocks in the resorption phase; oral cavity – rabbit lip with hard and soft palate defect, slightly hyperemic oropharynx; clear consciousness, tracks objects, sleeps intermittently, suspects occipital stiffness; breathing rate – 26/min, SpO₂ – 97%, heart rate = 120/min, T/A = 95/65 mmHg.

The presumptive diagnosis was established: Meningococcal infection. Meningococemia. Meningococcal meningitis. Lumbar puncture was performed with cerebrospinal fluid sampling. Blood, urine, cerebrospinal fluid, pharyngeal smears and eruptive elements were taken for bacteriological investigations.

The antibiotic treatment was continued with ceftriaxone, the pathogenetic one included dexamethasone. In continuation, the improvement

of the general condition of the child, the normalization of the body temperature was confirmed.

Nonspecific paraclinical investigations during treatment were as follows (tab. 1, 2):

Table 1. Blood count in dynamics.

Indicators / data	06.01.22	10.01.22	14.01.22
Hemoglobin (g/L)	94↓	114	108↓
Erythrocytes ($10^{12}/L$)	4.21	5.23↑	4.81
Platelets ($10^9/L$)	285	521↑	586↑
Leukocytes ($10^9/L$)	25.74↑	20.57↑	15.96↑
Unsegmented (%)	48↑	4	1
Segmented (%)	21	27	10
Eosinophils (%)	0↓	0↓	1
Lymphocytes (%)	25↓	54	65
Monocytes (%)	2.9	11.5	15↑
ESR (mm/h)	22↑	5	10

Table 2. Biochemical analysis of blood in dynamics.

Indicators / data	06.01.22	10.01.22	14.01.22
ALT (U/L)	251.9↑	101.8↑	78.7↑
AST (U/L)	78.7↑	38.3	50.0↑
Urea (mmol/L)	4.81	5.20	
Creatinine (mcmol/L)	36↑	59↑	73↑
Glucose (mmol/L)	8.61↑	5.43	4.45
Amylase (U/L)	13↓		
Prothrombin index (%)	97		

CSF from 06.01.22: slightly cloudy; Pandy's reaction - positive (+); cytositis - 37 cells/mcl, neutrophils - 55%, lymphocytes - 45%, protein - 0.33 g/L; unchanged erythrocytes - moderate amount; chlorides - 128.8 mmol/L; glucose - 5.80 mmol/L.

Chest radiograph from 06.01.22: lung pattern accentuated bilateral bronchovascular with bilateral perihilar peribronchovascular infiltrate. Reactive, structured pulmonary hila. Free pleural sinuses. Cord - normal.

Specific immunological paraclinical investigations (10.01.22): Anti-CMV-IgG - positive; Anti CMV IgM - positive; HBsAg - negative; anti-HCVsum - negative.

The bacterioscopic and bacteriological results of the cerebrospinal fluid, from the eruptions, from the pharynx, on the background of antibacterial therapy, were negative.

Bacteriological investigation of urine from 10.01.22: *Candida albicans* (susceptible to clotrimoxazole, fluconazole, ketokonazol, nystatin, etc.).

On 12.01.22, the preventive result of the bacteri-

ological investigation of the blood, taken on 06.01.22, was received, with the finding of an increase in the broth of gram-positive, catalase-negative cocci flora. To determine the germ, the automatic microbiological analyzer Vitek 2 was used: identified *Leuconostoc pseudomesenteroides*, sensitive to ampicillin, azithromycin, cefepime, chloramphenicol, clarithromycin, erythromycin, norfloxacin, tetracycline; intermediate sensitivity to ciprofloxacin, levofloxacin; resistant to cefotaxime, clindamycin, cotrimoxazole, vancomycin.

The final diagnosis was established: Acute meningococemia and meningococcal meningitis. Septicemia with *Leuconostoc mesenteroides*. Cytomegalovirus infection. Cytomegaloviral hepatitis. *Candida albicans* urinary tract infection. Rabbit lip with cleft palate, bilateral. Hemophagocytic anemia.

Considering the result of the blood culture and anti-CMV-IgM - positive, the decision was made to change the etiotropic treatment, namely: cancellation of treatment with Ceftriaxone, indicating Amoxicillin clavulanate and Viferon. In continuation, the child remained afebrile, became active, with improvement in appetite and sleep,

without finding deviations from normal during the objective examination. On 14.01.22, blood was taken for the repeated investigation of sterility: the result – negative. On the same date, the patient was discharged home in satisfactory condition.

DISCUSSIONS

Infections caused by *Leuconostoc spp.* are poorly studied. Available literature data allows reconsideration of its relationship with the human body. Thus, at present, *Leuconostoc spp.* can be

considered pathogenic for humans. The clinical case presented is of a child, presumed immunocompromised, confirmed with bacteremia with *Leuconostoc pseudomesenteroides*, which was associated with meningococcal infection with meningococemia and meningococcal meningitis, on the background of *Cytomegalovirus* infection in reactivation and immunosuppression. The timely choice of etiological treatment in the case of identification of *Leuconostoc spp.*, is a necessary condition for obtaining a positive clinical result.

CONCLUSIONS

1. The presented clinical case is the first case of infection with *Leuconostoc spp.* described in the Republic of Moldova.
2. The correct choice of etiological treatment allows the eradication of infection with *Leuconostoc spp.*

CONFLICT OF INTERESTS

The authors have no conflict of interest to declare.

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