Newborn infant with recovery after intestinal perforation complicated with severe Clostridium difficile infection

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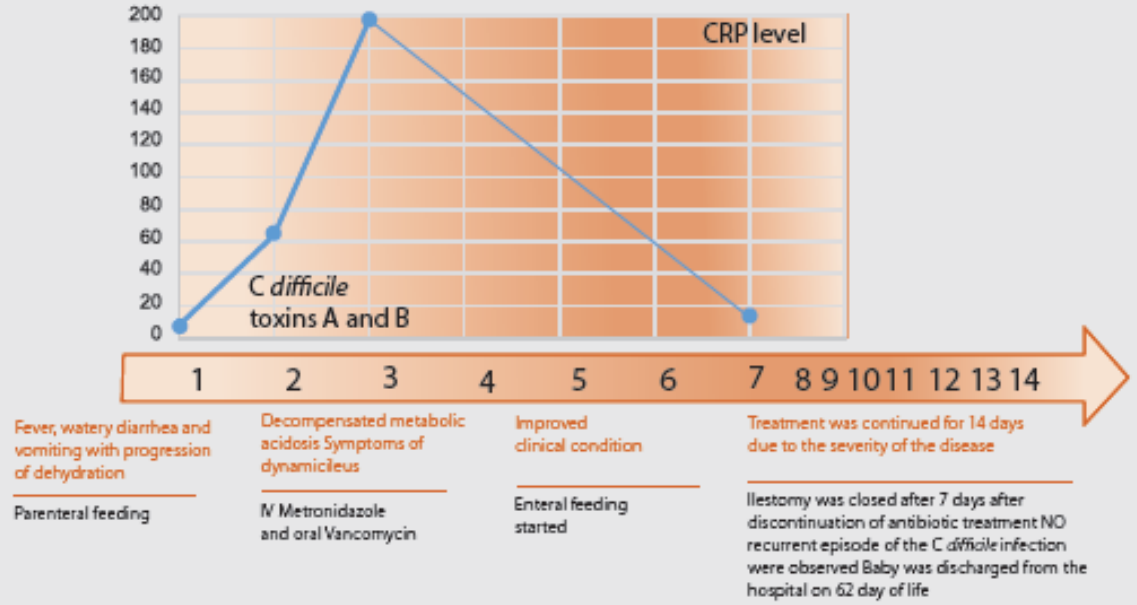
Background

Clostridium difficile is a Gram-positive, spore-forming bacteria found in soil, hospital environments, child care facilities and nursing homes. 15 to 63% of neonates are asymptomatic carriers of C *difficile* with the highest rate of colonisation in the NICU patients (33%), but also with the high prevalence in healthy outpatient and postnatal ward neonates (27 and 24% respectively). Wide spectrum antibiotic treatment, immunosuppression, surgery or manipulations, i.e. tube feeding, of GI are among the risk factors causing severe C *difficile* infection.

Case presentation

32-year-old gravida 2 para 1 mother. Polyhydramnios and fetal ascites identified on prenatal sonogram at 32nd GW. Emergency C-section was performed at 38th GW due to progression of fetal ascitis as well as deteriorating condition. 3,800 g infant boy was born with Apgar score 8/9. Surgery was performed on the 1st day of life, diagnosis of intrauterine peritonitis with intestinal perforation was confirmed and ileostomy formed. Antibiotics were administered until 15th day of life (cefuroxime 8 days, amikacin 7 days). Baby was transferred from NICU to step down neonatal department on the 10th day of life after reaching full enteral nutrition followed by parenteral nutrition with gradual increase of amount of maternal milk supplemented with probiotics. On the 25th day of life baby unexpectedly developed the symptoms of GI infection: fever, watery diarrhea and vomiting with progression of dehydration and decompensated metabolic acidosis, increased level of inflammatory markers. Blood and stool cultures, stool sample for viral antigens were negative. C *difficile* toxins A and B (enzyme immunoassay) were positive in the stool sample. Treatment with IV metronidazole and oral vancomycin was started and continued for 14 days due to the severity of the disease. Baby was discharged from the hospital on 62th day of life with no recurrent episodes of the C *difficile* infection.



Conclusions

We speculate, that intrauterine infection and intrauterine bowel perforation could be the initial determinant of affected microbiota and activation of the C *difficile* infection with acute gastrointestinal symptoms in our newborn baby. We could not to take into consideration long term use of broad spectrum antibiotics as another important factor responsible for the dysbiosis and activation of the C *difficile* infection. Identification of the C *difficile* toxins A and B, toxigenic culture or polymerase chain reaction should be used in neonates with acute gastrointestinal symptoms. Acute cases of the disease should be treated with combined antibiotic therapy including intravenous metronidazole and oral vancomycin as an optimal choice.

Bacterial aetiology of bloodstream infections and antimicrobial susceptibility among paediatric oncohaematologic patients

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Background and aims

Sepsis is the leading cause of morbidity and treatment-related mortality in patients with haematologic malignancies and solid tumours undergoing intensive cytotoxic chemotherapy (1). The emergence of carbapenem resistant Gram-negative and vancomycin resistant Gram-positive bacteria is occurring worldwide (2). Our aim was to analyse local species distribution causing bacteremia and their antibiotic resistance patterns in our oncohaematology centre in order to review the evidence based strategy for empirical antimicrobial therapy.

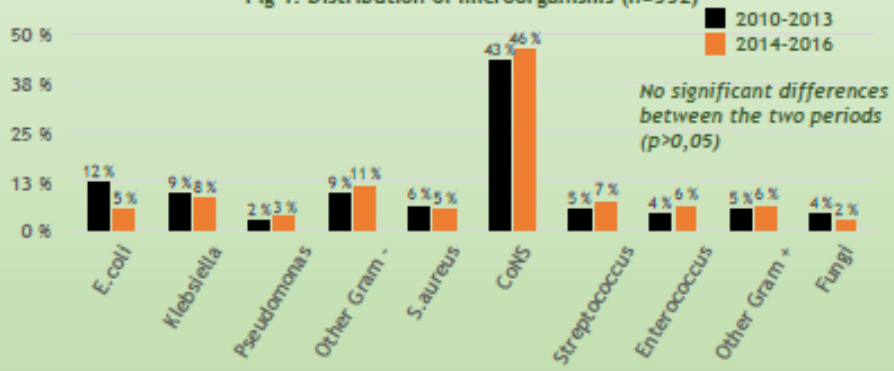
Material and methods

All positive blood cultures (n=460) of paediatric cancer patients treated at the Centre for Paediatric Oncology/Haematology, Children's Hospital, Affiliate of Vilnius University Hospital Santaros Klinikos during the recent 7 years (2010-2016) were retrospectively analysed. The data were compared between two periods: 2010-2013 and 2014-2016.

Results

A total of 532 microorganisms were cultured (67.7% gram-positive bacteria, 29.5% gram-negative bacteria and 2.8% fungi). Monospecies comprised majority (85.4%) of blood cultures. Two species grew in 62 cultures (13.5%) and three species - in five cultures (1,1%).

Fig 1. Distribution of microorganisms (n=532)



Other Gram-negative bacteria: *Acinetobacter baumannii, A. lwoffii, Aeromonas hydrophila, A. sobria, Agrobacterium radiobacter, Alcaligenes spp., Altenaria spp., Bacteroides ureolyticus, B. vulgatus, Enterobacter aerogenes, E. cloacae, Haemophilus parainfluenzae, Moraxella catarrhalis, Pantoea spp., Salmonella enteritidis, Stenotrophomonas maltophila, Veilonella spp.*
Other Gram-positive bacteria: *Actinomyces viscosus, Aerococcus viridans, Bacillus spp., Bifidobacterium spp., Clostridium tyrobutyricum, Corynebacterium spp., Micrococcus luteus, M. lylae*
CoNS - coagulase negative Staphylococci

Table 1. Gram-positive bacteria antimicrobial susceptibility.

Bacteria	CoNS (n=238)			S. aureus (n=30)			Streptococci (n=33)			Enterococci (n=28)		
Period	2010-2013	2014-2016	Total	2010-2013	2014-2016	Total	2010-2013	2014-2016	Total	2010-2013	2014-2016	Total
Erythromycin	37%	29%	33%	77%	100%	87%	46%	54%	50%	-	-	-
Gentamicin	50%	49%	50%	94%	100%	97%	-	-	-	50%	50%	50%
Linezolid	97%	95%	95%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Oxacillin	19%	28%	23%	100%	100%	100%	-	-	-	-	-	-
Penicillin	5%	7%	6%	29%	42%	35%	79%	61%	69%	-	-	-
Teicoplanin	54%	55%	54%	100%	100%	100%	-	-	-	100%	100%	100%
Vancomycin	95%	94%	95%	90%	100%	93%	93%	100%	97%	80%	100%	92%

The most important and the most commonly used antimicrobials among childhood cancer patients are highlighted. Sensitivity ≥ 80% Sensitivity <80%

Table 2. Gram-negative bacteria antimicrobial susceptibility.

Bacteria	Klebsiella (n=45)			Pseudomonas (n=14)			E.coli (n=46)			Other gram negative bacteria (n=52)		
Period	2010-2013	2014-2016	Total	2010-2013	2014-2016	Total	2010-2013	2014-2016	Total	2010-2013	2014-2016	Total
Amikacin	91%*	65%*	79%	86%	100%	93%	100%	100%	100%	90%	95%	93%
Amoxiclav	35%	25%	30%	-	-	-	64%	80%	67%	57%*	17%*	42%
Ceftazidime	33%	32%	33%	100%	100%	100%	91%	100%	93%	63%	50%	57%
Ciprofloxacin	41%	35%	38%	100%	86%	93%	88%*	55%*	79%	79%	76%	78%
Gentamicin	48%	55%	51%	100%	100%	100%	85%*	55%*	77%	81%	62%	71%
Imipenem	100%	100%	100%	100%	100%	100%	100%	100%	100%	92%	100%	95%
Meropenem	100%	100%	100%	80%	100%	92%	100%	100%	100%	91%	100%	95%
Piperacillin/ Tazobabactam	57%	30%	44%	71%	57%	64%	91%	82%	89%	71%	50%	63%
Tobramycin	35%	17%	28%	83%	100%	92%	83%	60%	79%	78%	67%	73%
Co-trimoxazole	27%	20%	24%	-	-	-	19%	9%	17%	52%	70%	61%

The most important and the most commonly used antimicrobials among childhood cancer patients are highlighted. Sensitivity ≥ 80% Sensitivity <80%
* Significant changes during the time periods (p<0.05)

Conclusions

Gram-positive bacteria were the most frequent cause of bloodstream infection, with a predominance of coagulase-negative staphylococci.
Resistance to ciprofloxacin was high and increasing which resulted in abolishing of ciprofloxacin prophylaxis for stem cell transplanted patients.
Due to a high resistance pattern among Gram-negative bacteria, carbapenems are the first-line choice in febrile neutropenia for the highest risk patients, however, susceptibility pattern has to be closely monitored.
There was no emergence of vancomycin resistant Gram-positive bacteria, however appropriately use of glycopeptides is essential.

1. Penack O, Becker C, Buchheidt D, et al. Management of sepsis in neutropenic patients: 2014 updated guidelines from the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology (AGIHO). *Annals of Hematology*. 2014;93(7):1083-1095.
2. Ventola CL. The Antibiotic Resistance Crisis: Part 1: Causes and Threats. *Pharmacy and Therapeutics*. 2015;40(4):277-283.

Human Enteroviruses Isolated from Stool Samples of Patients Hospitalised at Children's Hospital*

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Background: Lithuania, along with the World Health Organization (WHO) European region, was certified polio free by the Regional Commission for the Certification of Poliomyelitis Eradication in 2002. The last poliomyelitis case due to indigenous wild poliovirus occurred in Lithuania in 1972.

The main strategy recommended by the WHO for PV surveillance is the investigation of acute flaccid paralysis (AFP) cases in children, which is a sensitive marker for poliomyelitis.

Poliovirus transmission is prevented by achieving and maintaining high immunization coverage. Surveillance of AFP cases among children below 15 years of age and appropriate level of proficiency of laboratory of virology are important components of the programme of polio eradication. Following the WHO recommendations, in Lithuania National public health surveillance laboratory processes the stool samples from hospitalized individuals with AFP and clinically suspected enterovirus infection. Polio suspected isolates are further analysed at the WHO Enterovirus RRL in Helsinki. Such a system ensures a high level of clinical vigilance and laboratory proficiency.

Aim of this study was to analyse the results of virological testing of samples collected at Children's hospital Paediatric Centre from the AFP and clinically suspected enterovirus infection.

Methods: Retrospectively case histories were analysed if the patient met the following criteria: 1. Hospitalised at Children's hospital Paediatric Centre between January 2014 – October 2017; 2. Stool samples were collected for suspected enterovirus infection (acute cutaneous eruptions, mucosal membrane lesions, mild respiratory illness, CNS involvement) or acute flaccid paralysis (AFP); 3. Stool samples were processed at National Public Health Surveillance laboratory; 4. The data about patients age, clinical features and indications for stool sampling were collected.

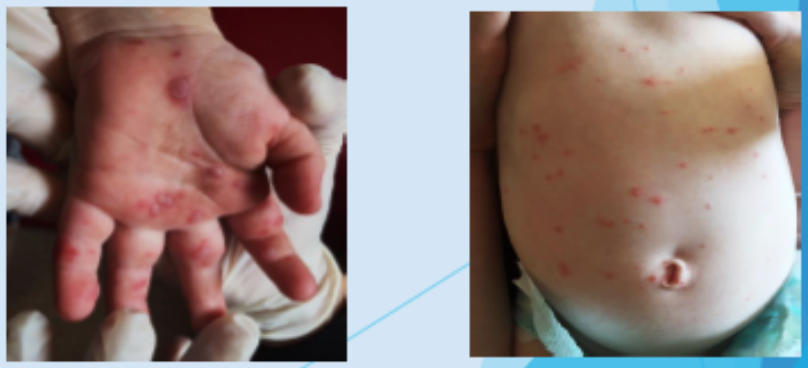
Department	№ Of Samples	Diagnosis
The Children's Infectious Disease Department	136	Exanthems and enanthems
	5	Encephalitis
	3	Meningitis
The Paediatrics Department	3	Myopericarditis
	1	Meningitis
The Children's Neurology Department	5	Flaccid paraplegia
	2	Meningitis
	3	Transverse myelitis, Guillain-Barré syndrome
The Children's Pulmonology and Allergology Department	33	Exanthems and enanthems
	4	Meningitis
In total:	195	

TABLE 1 № Of stool Samples collected from different departments of Paediatric Centre

Results: In total, 195 stool samples from 117 patients, hospitalised at Paediatric Centre were analysed (table 1). In 5 patients with AFP no polio or other enteroviruses were isolated during 2.5 years of surveillance. Enteroviruses were isolated in 12 out of 117 patients with clinically suspected enterovirus infection. Mean age of EV positive children with symptoms was 2 years (range: 166 days-7 years; median age: 18 months). No wild polioviruses were isolated in these patients. In one 10-month-old child, Sabin-like poliovirus type 3 was detected in two stool samples. He was hospitalised because of high-grade fever and maculopapular rash on the trunk, extremities. The boy was fully vaccinated for his age according to NIP (which includes 3 doses of Inactivated Polio Vaccine (IPV) vaccine). He attended a nursery. There was no travel abroad history or known contact with Oral Polio Vaccine (OPV) vaccinated persons from foreign countries. No other enteroviruses were isolated in this patient.

Presence of non-polio Enteroviruses was recorded in 11.6% (22/190) of stool samples. Nonpolio human enteroviruses isolated from stool samples belonged to species: coxsackievirus A10 (8 samples), coxsackievirus A16 (2 samples), coxsackievirus A 4 (1 sample), coxsackievirus B1-6 (4 samples), echovirus 6 (3 samples) and enterovirus non typable (2 samples). 90% of positive stool samples were isolated from patients who reported nonspecific acute febrile illnesses with petechial or purpuric rash. One non-polio EV-positive child was reported with sepsis like disease.

Conclusions: 1. No wild-type polioviruses were isolated during the study period. 2. Our experience shows that Sabin-like polio-viruses might circulate even in a community where OPV is not in use and without evident contact with OPV vaccinated person. 3. It is important to guarantee high-quality surveillance to maintain polio-free status until global eradication is achieved. 4. The most commonly isolated enterovirus was coxsackievirus A10. 5. In most cases the diagnosis of EV infection is based only on clinical findings as laboratory confirmation is very scarce.



Pictures of patients with laboratory confirmed EV infection

Acknowledgements: We thank Svajūnė Muralytė, Head of theVirological testing subdepartment, National Public Health Surveillance Laboratory for providing information about enterovirus samplings.

FUO

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10th November 28-29 Lithuania, Vilnius

History

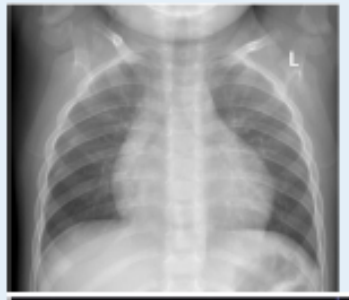
- 19/12 ♀, ↑ T for 16 days
- no accompanying symptoms
- treated in regional hospital with cefuroxime, meropenem
- increased GOT, GPT (reactive/drug-induced hepatitis?)

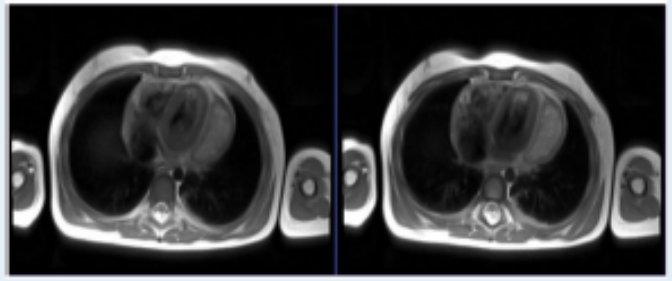
Treatment

- ethambutol (25 mg/kg)
- levofloxacin (20 mg/kg)
- amikacin (20 mg/kg)
- cycloserine not available

ATS/CDC/IDSA Clinical Practice Guidelines for Drug-Susceptible TB, CID 2016; 63: 181

Investigation





- cardiac surgery: caseous structure
- direct microscopic preparation and culture

Mycobacterium tuberculosis

Take home message

Etiological factor	Developed countries	Developing countries	Together
Bacterial infection			
Brucellosis	7	97	104
UTI	20	41	61
Tbc	22	39	61
Typhoid	7	47	54

Chow A, Robinson JL. Fever of unknown origin in children: a systematic review. World J Pediatr. 2011; 7: 5-10

Final diagnosis

tuberculous pericarditis